CONTENTS

THE STRUCTURE OF NORMAL FIBERS OF PURKINJE IN THE ADULT HUMAN HEART AND THEIR PATHOLOGICAL ALTERATION IN SYPHILITIC MYOCARDITIS

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I. INTRODUCTION

Early in 1917 we received from Dr. Edward P. Carter the heart of a syphilitic man 42 years of age. The patient had succumbed to cardiac trouble, showing the characteristic clinical symptoms of atrial fibrillation in the course of chronic myocarditis associated with bizarre *aberrant* electrocardiograms. The fixation of this material received within an hour of the death of the patient was carried out under most favorable conditions. The histological examination of the preparations revealed profound pathological changes in the atrio-ventricular bundle. But in order to interpret with certainty the nature and extent of the alterations it was necessary to compare these preparations with others from the normal heart of a man of about the same age. Such material was furnished to us some weeks later by Dr. Carter. One of his patients, a strong vigorous man of 36 years, in whom all possibility of heart disease could be excluded, died of pneumonia. An autopsy was performed immediately after death and the heart received in the laboratory while still warm.

We have then two perfectly fresh hearts belonging to men of practically the same age, the one pathological and the other normal. We propose here to set forth all the observations which we have been able to make upon this valuable material.

It would have been interesting, had it been possible, to study the evolution of the fibers of Purkinje from the earliest embryonic stages up to the age of 70 to 80 years, but at present we have not the necessary material. Nevertheless we are able to present certain new facts in the morphological study of the fibers of Purkinje in the adult. These facts also permit us to evaluate correctly the pathological alterations in the diseased specimen.

The fibers of Purkinje have been made the subject of many researches. But the evolution of the constituent parts of the atrio-ventricular bundle in man is relatively little understood. Marceau (1902) has published an excellent work upon the development of the Purkinje fibers in the sheep, both in embryonic stages and in young and adult subjects. But it is obvious that the stage of evolution of this element in a sheep of two years (plainly an adult) is not to be compared with that in a child of the same age. Tawara (1906) has published interesting observations upon the heart of mammals and upon a series of human hearts, embryo, child and adult. One must insist upon the absolute necessity of comparing the structure of the pathological bundle with that of the normal bundle at the same age. Some authors have had at their disposal abundant material. Thus Mönckeberg (1908) was able to utilize the hearts of numerous embryos, children, adults and old persons and also 70 pathological hearts, but gave scant attention to the description of a fiber of Purkinje as described in the text-books of histology. In describing the muscular fibers of the atrio-ventricular bundle he speaks of nuclei situated "in zentralen-röhren-förmigen Vakuolbildungen," of fibers of Purkinje "auf weite Strecken hohl" and of others with "nur schmale ovale Hohlräume," of "Hohlfasern," of "soliden Fasern" and of "einzelne Faser teils hohl, teils solid." Descriptions of this character serve to obscure the problem rather than to clarify it.

In the following account one of us (T. W. T.) is responsible only for the description of gross morbid anatomy and for the rendering of the English text. The senior author (O. V. d. S.) has conducted the entire histological investigation and is responsible for the observations made and the conclusions reached.

II. POST-MORTEM EXAMINATION OF HEARTS

Heart 1 was received from Dr. Carter in February, 1917. It was still warm upon arrival and the gross examination was made at once in the laboratory.

The heart is that of a colored male patient (S. S.) of 42 years. The weight of the organ is 770 gm. It is much enlarged: the length from root of pulmonary artery to apex is 125 mm. The amount of fat is not increased. There are large "milk spots" on both ventricles. The pericardium is normal. The right and left atria are large and their walls thick, but neither shows the marked enlargement and hypertrophy

apparent in the ventricles. The right wall of the right atrium at the lower end of the crista terminalis measures 5 mm. in thickness; that of the left atrium immediately above the orifices of the pulmonary veins is also 5 mm. thick. The actual muscular wall of the right ventricle (not including any of the prominent trabeculæ carneæ) between the papillary muscles is 6.5 mm. in thickness and the diameter of the wall of the left ventricle in a corresponding situation measures 16 mm. Near the atrio-ventricular junction the cross-section of the right ventricular wall is 7 mm. and that of the left ventricle 20 mm. There is no apparent endocarditis. The cusps of all four valves are free and normal. The right atrio-ventricular orifice admits four fingers: into the left the entire five can be passed as far as the proximal interphalangeal joint. The orifices of both coronary arteries are surrounded by atheromatous patches which are also numerous in the commencement of the aorta. There is marked enlargement of the ventricular trabeculæ and papillary muscles.

On opening the right side a well-marked pars membranacea septi is to be observed, in the lower margin of which the bundle can be fairly well seen. Immediately in front of the fibrous septum there is marked cicatrization along the course of the bundle, which can be identified under the endocardium right into the moderator band and so to the anterior papillary muscle. In the right atrium strands of Purkinje fibers are visible upon the septal wall, passing from the upper part of the crista toward the atrio-ventricular junction. Similar bands terminating in the same location can be seen running from the region of the coronary orifice. Blocks of tissue about 10 mm. square and 5 mm. thick were cut from the several areas recorded below. In removing such blocks of tissue it is sometimes difficult to be sure that the Purkinje fibers have been included, especially if they lie deeply in the myocardium. If the cut edge of the block be examined promptly, however, the retraction of the Purkinje bundles, always greater than that of myocardial fibers in the perfectly fresh organ, brings about a localized dimpling of the cut surface which immediately sets all doubts at rest. In this part we were particularly fortunate in observing the dimpling in every piece removed except in Nos. 4 and 5 where much cicatrization had occurred.

On opening the left ventricle the bundles show less definitely. The anterior and middle limbs immediately disappear among the unusually marked trabeculæ and no attempt was made to secure these. The

posterior branch is plainly visible in its course toward the posterior papillary muscle and portions of it were obtained as stated below. No histological examination was made of the left atrium.

In referring to the cusps of the aortic valve we shall not employ the usual terms, but adopt Keith's method of calling them right coronary, left coronary and non-coronary, respectively, in reference to the particular artery which arises above each.

The branches of the coronary vessels in the atrio-ventricular junction and those passing along the main branches of the Purkinje system are not obvious to the naked eye in this heart.

After the tissue blocks had been removed from the heart the entire organ was photographed (Figs. 64, 65) and then preserved by the Kaiserling method.

The following is a list of the sites from which tissue blocks were removed in Heart 1:

RIGHT VENTRICLE AND ATRIUM

Piece 1. Moderator band (trabecula supraventricularis) near base of anterior papillary muscle.

Piece 2. Anterior papillary muscle at site of entrance of moderator band.

Piece 3. Right branch of bundle on septal wall proximal to moderator band.

Piece 4. Stem of bundle under endocardium of right ventricle beneath septal cusp of tricuspid valve. This portion includes the commencement of the right and left main branches. It shows marked cicatrization.

Piece 5. Pars membranacea septi immediately above and behind Piece 4, but unlike the latter, which is from the interventricular part of the septum, this is from the septum between the right atrium and the left ventricle.

Piece 6. Tissue of the coronary groove of the right atrium immediately above and including the margin of the orifice of the coronary sinus.

Piece 7. Part of the septal wall of the right atrium immediately adjacent to the non-coronary cusp of the aortic valve.

Piece 13. Piece of ventral wall of right ventricle for myocardial fibers.

Piece 14. Interatrial septum between coronary orifice and fossa ovalis including the margin of the latter. This block is from the wall above and behind Piece 6.

Piece 15. Block from right atrial wall adjoining the orifice of the superior vena cava and including the upper extremity of the crista terminalis and the muscular ring at the junction between atrial canal and atrial appendix. From this block Pieces 16 and 17 were divided off.

LEFT VENTRICLE

Piece 8. Left branch of the atrio-ventricular bundle immediately below the right coronary cusp of the aortic valve before the bundle has broken up into its three left constituent limbs. This block contains the bundle where it first appears under the endocardium of the left ventricle.

Piece 9. Left posterior branch of the bundle in the septal wall. This was the only branch visible to the naked eye in the left ventricle of this heart.

Piece 10. Continuation of left posterior branch passing among the trabecular tissue between septal wall and posterior papillary muscle.

Piece 11. Base of the posterior papillary muscle at its point of union with the trabecula containing the left posterior branch of the bundle.

Piece 12. Block from the ventricular wall at the base of the anterior papillary muscle for myocardial fibers.

Heart 2 was received from Dr. Carter on April 10, 1917. It was still warm upon arrival and the gross examination was made at once in the laboratory.

The heart is that of a white male (H. T.) of 36 years, who succumbed to an attack of acute pneumonia. The weight of the organ is 240 gm. It is of normal size and appearance. The length from root of pulmonary artery to apex is 97 mm. There is a considerable but not abnormal amount of fat. Several "milk spots" are visible on both ventricles. The pericardium is normal. The right and left atria are of normal size. The wall of the right atrium at the lower end of the crista measures 4 mm. in thickness: that of the left atrium immediately above the orifices of the pulmonary valves is 3 mm. thick. The actual wall of the right ventricle between the papillary muscles is 6 mm. in thickness, but at least half of this is fat. The diameter of the wall of the left ventricle in a corresponding situation is 11 mm., only about

1 mm. of this being due to fat. Near the atrio-ventricular junction the cross-section of the right ventricular wall is 12 mm., 4 mm. of this being fat, and that of the left ventricle 11.5 mm. (all muscle). There is no apparent endocarditis. All the orifices and valvular cusps in this heart are of normal size and appearance. The orifices of the coronary arteries are normal and there is no atheroma of the aorta.

On opening the right side the Purkinje system is much less plainly seen than in Heart 1 and the right ventricular bundle is deeply embedded in the myocardial tissue. There is no pars membranacea septi. Blocks of tissue were taken according to the method adopted in Heart 1, as indicated below, and in most of these the Purkinje systems were identified by naked eye examination of the cut surface.

As in Heart 1 blocks of tissue were removed from the main left ventricular bundle and from its posterior branch.

The arterial circle at the right atrio-ventricular junction is plainly marked, the vessels being normal in thickness and in the appearance of the walls.

After the tissue blocks had been removed, the heart was preserved by the Kaiserling method. No photographs were taken.

The following is a list of the sites from which tissue blocks were removed in Heart 2:

RIGHT VENTRICLE AND ATRIUM

Piece 1. Moderator band (as in Heart 1).

Piece 2. Anterior papillary muscle (as in Heart 1).

Piece 3. Right branch of bundle (as in Heart 1).

Pieces 4, 5. Atrio-ventricular septum crossing right atrio-ventricular junction and including tissue corresponding to Pieces 4 and 5 of Heart 1. There is no pars membranacea septi in this heart.

Pieces 6, 14. Only one block of tissue was taken from the right atrial wall above the coronary orifice: it corresponds more to Piece 14 than to Piece 6 in Heart 1.

Piece 7. Part of the septal wall of the right atrium (as in Heart 1).

Piece 13. Ventral wall of right ventricle (as in Heart 1).

Piece 14. See above under Piece 6.

Piece 15. Right atrial wall adjoining orifice of superior vena cava and including the upper extremity of the crista terminalis (as in Heart 1). This piece was not subdivided as in Heart 1.

LEFT VENTRICLE

Piece 8. Left branch of the atrio-ventricular bundle immediately below the right coronary cusp of the aortic valve at the point where the bundle is breaking up into its three left constituent limbs. The piece corresponds to Piece 8 of Heart 1, except that it does not include, in all probability, the most anterior Purkinje fibers.

Piece 9. Left posterior branch of the bundle in the septal wall. This was the only branch visible to the naked eye in the left ventricle of this heart.

Piece 10. Continuation of left posterior branch (as in Heart 1).

Piece 11. Base of the posterior papillary muscle (as in Heart 1).

Piece 12. Block from the ventricular wall at the base of the anterior papillary muscle (as in Heart 1).

III. METHODS

We removed from both pathological and normal hearts pieces of the atrio-ventricular bundle at different levels. Each of these was numbered and Figs. 66 and 67 show the precise situations from which they were removed. Nos. 1, 2, 3, 4, 5, from the right ventricle; Nos. 6, 7, 14, 15, 16, from the right atrium; Nos. 8, 9, 10, 11, from the left ventricle; Nos. 12 and 13 are pieces of the myocardium for comparison with the cardiac tissue surrounding the atrio-ventricular bundle.

Each piece from the pathological heart has been cut into halves at right angles to the bundle. One of these in each instance was immersed in an osmic acid fixative, Flemming's or Hermann's solution, and the other in a non-osmic solution, Bouin's fluid or a 5% aqueous solution of trichloracetic acid.

The pieces of the normal heart were not subdivided: they were fixed entire either in an osmic acid solution or in a reagent of the second type. The period of fixation was one week for Flemming's solution, two days for Hermann's, 24 hours for Bouin's fluid and for trichloracetic acid. Pieces fixed in the two last-mentioned reagents were hardened in 70% alcohol, to which were added a few drops of tincture of iodine which is an excellent mordant for final staining. Before embedding in paraffin they were colored *en bloc* with borax carmine.

After embedding the pieces were cut in part at right angles to the axis of the atrio-ventricular bundle and in part tangential to the endocardial surface. These last preparations present many advantages and frequently show the beautifully plexiform arrangement of the Purkinje cells.

For staining reagents the following methods were used: After fixation with Bouin's fluid or trichloracetic acid one series of sections was colored with iron hæmatoxylin and Congo red, another by Mallory's method. Sections fixed in osmic reagents were stained, some with safranin and light green, others with iron hæmatoxylin and Congo red and others again by Mallory's method.

All the figures reproduced (Plates 1 to 12) represent photographs taken with the Bausch and Lomb Photomicrographic Camera G1. It would have been preferable to use colored figures in order to simplify description and to bring out more clearly the difference in appearance of the constituent parts of the muscular elements and the interstitial connective tissue. It is often difficult to appreciate in a photograph what belongs to the Purkinje cell and what should be considered as endomysium or perimysium. These features, however, are perfectly clear in the preparations. We shall attempt to remedy this defect, at least in part, by indicating precisely the elements most important from the point of view of our description. Photography on the other hand offers a very great advantage, in that it reproduces faithfully and much better than any drawing the morphological appearance of the different varieties of Purkinje fibers, some more or less embryonic in type, some more advanced in their evolution representing stages of transition towards cardiac fibers, and also of myocardial fibers properly so called.

We do not intend to describe the topography of the atrio-ventricular bundle, but shall content ourselves with making a histological study of Purkinje fibers in the normal heart, emphasizing the different stages in their evolution and the characters in which they differ from cardiac fibers at various levels of the atrio-ventricular bundle. By this study we shall be able to determine that in the pathological heart the Purkinje cells undergo an identical evolution carried, however, to pathological excess even to the point of atrophy and complete disappearance.

In order to avoid minute description of different parts of the atrio-ventricular bundle we give a tabular summary indicating approximately the thickness of the endocardium, the existence of smooth muscular fibers in its substance, the diameter of the cells of Purkinje, their tendency to form meshworks or cellular plexuses, the occurrence of intercalated discs, the thickness of the perimysium and endomysium and the degree of interstitial inflammation in the pathological heart.

TABULAR SUMMARY

A. NORMAL HEART (2)

Piece	Endocardium		Cells and Fibers of Purkinje			
	Thickness	Smooth fibers	Transverse diameter	Plexus	Intercal. discs	Perimysium, Endomysium
1	Thin.	Few.	Considerable.	Present.	Visible.	Thin.
2	Thin.	Isolated bundles.	Medium and thin.	Present.	Visible.	Thin.
3	Thin.	None.	Medium and thin.	Present.	Visible.	Thin.
4	Thin.	More or less continuous layer.	Considerable.	Plexus of cardiac cells.	Visible.	Thin.
5	Thin.	As in 4.	Considerable.	Whorls and plexus.	Very plain.	Thin.
6	Thick.	Two layers in places.	Medium.	Present.	Very plain.	Thin.
7	Thick.	Few.	Medium.	Present.	Very plain.	Thin.
8	Medium.	More or less continuous layer and isolated bundles.	Thick, medium and thin.	Whorls and plexus.	Very plain.	Slightly thickened.
9	Thin.	Few.	Thick, medium and thin.	None.	Very plain.	Thin.
10	Thin.	Few.	Thick and medium.	Present, partly cardiac and partly Purkinje cells.	Very plain.	Thin.
11	Medium.	Few.	Thick and medium.	Present.	Very plain.	Thin.
15	Medium.	Two layers in places.	Thin and medium.	Present.	Visible.	Thin.

B. PATHOLOGICAL HEART (I)

Piece	Endocardium		Cells and Fibers of Purkinje				Inflammation in the atrio-ventricular bundle
	Thickness	Smooth fibers	Transverse diameter	Plexus	Intercal. discs	Perimysium, Endomysium	
1	Medium.	None.	Thick, medium and thin.	None.	None.	Thick.	Diffuse.
2	Thin.	None.	As in 1.	Present.	Visible.	Thick.	Diffuse.
3	Medium.	None.	Some thick, more medium and thin.	Present with some whorls.	Visible.	Thick.	None.
4	Thin and thick.	None.	Trunk: Some medium, others thin; lateral bundles: thick, medium, thin.	None.	Visible.	Thick.	None.
5	Thin and thick.	None.	Most thick, some medium and thin; trunk (mode): some medium, others very thin.	Present, partly cardiac and partly Purkinje cells. Whorls.	Visible.	Thick.	Slight.
6	Medium and thick.	Isolated bundles.	Medium and thin.	None.	None.	Slightly thickened.	Slight.
7	Thin and medium.	None.	Medium and thin.	Present.	None.	Thick.	None.
8	Medium.	Isolated bundles.	Medium and thin.	Present.	Very plain.	Thick.	Diffuse.
9	Medium.	None.	Medium and thin.	Present.	Very plain.	Very thick.	Well marked.
10	Medium.	Isolated bundles.	Thick, medium and thin.	Present.	Very plain.	Very thick.	Well marked.
11	Thick.	Isolated bundles.	Thick, medium and thin.	None.	Very plain.	Very thick.	Well marked.
14	Thick.	Isolated bundles.	Thick, medium and thin.	Present.	Visible.	Thick.	Slight.
15	Thin and medium.	Isolated bundles.	Medium and thin.	Purkinje plexus; cardiac plexus.	None.	Slightly thickened.	Slight.
16	Thin and thick.	Isolated bundles.	Medium and thin.	None.	None.	Slightly thickened.	None.

IV. BIBLIOGRAPHY

In 1839 and 1845 Purkinje discovered in the heart musculature the cells which still bear his name, but he did not observe them in man. Since this time several authors, among them Aeby (1862), Obermeier (1866), Lehnert (1868), Frish (1869), Krause (1876), Duval (1897), Minervi (1899), and Hofmann (1902) have denied their existence in the human heart. Indeed in 1907 Fahr affirmed that in the human embryo there is no difference in structure between the constituent parts of the atrio-ventricular bundle and those of the myocardium.

Most histological text-books, especially those of France and Germany, state that Purkinje fibers are absent from the human heart. This statement is undoubtedly based upon the negative findings of the foregoing authors and ignores the positive results of others, notably Schweigger-Seidel (1871), Henle (1876), Gegenbauer (1877), and Romiti.

To Tawara (1906) belongs the credit for demonstrating in the heart of the sheep, the dog and man, that the bundle of His divides into two ventricular branches, right and left, which are continuous with fibers of Purkinje in the terminal expansions of the atrio-ventricular bundle. Although this author demonstrates marked differences in structure between cells everywhere in the bundle and myocardial cells, he reserves the term fibers of Purkinje specially for those constituent parts of the terminal expansions in the heart of the sheep. Since this time the majority of authors have followed Tawara's example, but give the name " fibers of Purkinje," however, to the fibers of the terminal expansions in the mammalian and in the human heart. They designate as muscular fibers the constituent parts of other segments of the bundle, especially of its atrial part, of the stem and of its two branches. We shall term cells and fibers of Purkinje the muscular elements of the entire atrio-ventricular bundle.

Through numerous published investigations one is enabled to recognize the essential morphological characters of the Purkinje cells in the hearts of adult mammals. They are bulky, of polyhedral or prismatic shape, and are massed together to form the bands known as Purkinje fibers. Ranvier (1876) has shown that they are united to each other by a scanty intercellular cement which is soluble in a 40% caustic potash solution and is stained black by silver nitrate.

Marceau (1902) differentiates in the sheep three varieties of Purkinje cells according to their shape.

1. Spherical or polyhedral elements. This type of cell is polyhedral near the axis of the muscular bundle and spherical near its periphery. They measure from 20 to 100 μ in diameter.

2. Irregularly polyhedral cells situated in the center of the bundle.

3. Fusiform cells in the finer fibers which are continuous with the cardiac fibers. These cells measure 80 to 150 μ in length and 15 to 35 μ in diameter.

According to all authors, even the earliest, v. Hessling (1854), Eberth (1866), Obermeier (1867), Schweigger-Seidel (1871), Ranvier (1876), the elements are polynuclear. Marceau found in them one or two nuclei as a rule and, when two were present, they were ovoid and close together, or occasionally united to form a single mass. Not rarely one finds three, four, five or even six nuclei of different sizes in one cell. The cytoplasm is represented by a central axial mass, the sarcoplasm or indifferent protoplasm, devoid of contractile fibrils, in which v. Hessling has described fatty and pigment granules. This is surrounded by a more compact peripheral layer variable in thickness, in which appear myofibrils in greater numbers as the embryo or the animal increases in age. These indeed may develop even in the central zone but are much rarer there. Obermeier distinguishes three forms of Purkinje cells:

1. Spheroidal cells with a finely striated cortex and an abundant protoplasm. They contain two or three nuclei.

2. Cells more elongated, with a cortex thicker and more obviously striated and with less abundant protoplasm. Their nuclei are fewer in number.

3. Other cells even more elongated, more slender and with a striated cortex occupying almost the entire thickness of the cell body. These cells are gradually continuous with ordinary cardiac fibers.

Many authors describe the occurrence in Purkinje cells of glycogen droplets. Mönckeberg (1908) attaches great importance to their presence. He affirms that the expansions of the left branch in the heart of the child are continuous with Purkinje fibers, which are very closely similar to neighboring cardiac fibers. The presence of glycogen alone affords a certain criterion for the determination in this part of the atrio-ventricular bundle whether a cell is a Purkinje element or a true cardiac muscle cell. Cardiac cells contain no trace of glycogen.

Marceau (1902) and Schockaert (1909) describe in the Purkinje cell of the sheep four layers:

1. A central zone absolutely unstained, enclosing the nuclei. Hoyer (1901) and Marceau considered this area as an artefact resulting from shrinkage induced by reagents.

2. A granular layer surrounding the foregoing, dotted throughout with rounded granules of variable size and staining intensely with iron hæmatoxylin.

3. A stratum uniformly colored pale grey, in which very fine isolated fibers may be distinguished but of which the transverse striation is scarcely perceptible.

4. A striated cortex formed by bundles of myofibrils arranged in a circular, oblique or longitudinal manner. Schockaert describes certain enigmatic formations in the central sarcoplasm, striated or comb-like plates, to the number of two, three or even more. They are formed by an axial, moniliform or granular rod with a great number of laterally directed filaments each of which passes through one of the axial granules. There is complete agreement among all authors regarding the continuity of the myofibrils across the intercellular spaces and across many cellular areas. According to Lehnert (1868), Frish (1869) and Schmaltz (1886), the Purkinje fibers are represented by two absolutely distinct parts. There is a network formed by fibrils and fibrillar bundles intercrossing in different directions. This network of fibrils is produced by and in continuity with the cardiac fibers. It is independent of a second type of elements, the "granule-cells" or "the granules" which fill the spaces of the network. In the interior of these "grains" myofibrils never appear, according to Schmaltz. These authors have misunderstood the striated cortical layer of the Purkinje cells, yet they have always observed the continuity of the myofibrils passing longitudinally in the fibers described later with greater exactitude by Renaut (1893), Schäfer (1893), v. Ebner (1900), Hoyer (1901), Hofmann (1902), Marceau (1902), Tawara (1906), Mönckeberg (1908), De Witt (1909), Jordan and Banks (1917) and others. Renaut was the first who set himself to follow the exact course of the myofibrils. He distinguishes two systems in the bundles of Purkinje.

1. The superficial system or "feuillets musculaires superficiels" corresponding to Lehnert's enveloping retiform system. These superficial muscular sheets completely surround the peripheral cells of the bundle of Purkinje fibers. The fibrils in these sheets are parallel with each other and with the outline of the cells.

2. The deep system or " feuillets musculaires profonds " independent of the foregoing and represented by muscular columns or sarcostyles parallel with the axis of the bundle. One may follow these from cell to cell without interruption other than the line of intercellular cement. They traverse and intersect the superficial system and the more simple the bundles of Purkinje fibers become the more these sarcostyles increase in importance, while on the other hand the superficial sheets dwindle and disappear.

Marceau distinguishes in a Purkinje bundle, five or six cells in thickness, three varieties of myofibrils at least:

1. The longitudinal muscular layers of Renaut with rectilinear or slightly sinuous fibrils parallel with the axis of the bundle. They are very numerous in the axis itself and diminish in number regularly toward the surface of the bundle.

2. The " feuillets musculaires transversaux " or layers of fibrils arranged at right angles or obliquely toward the axis of the bundle. They intercross with each other and with the longitudinal fibrils. They form loops enveloping either the free surface of cells which bound the bundle or the surface of deeper cells.

3. Isolated fibers whose direction runs in general parallel to the cell outlines. They possess embryonic characters and are destined to be transformed into fibrils of the second variety. Where the bundle becomes thinner and continuous with a bundle of cardiac fibers its constituent cells elongate and become fusiform. The layer of transversely or obliquely arranged fibers atrophies more and more and the longitudinal group increases correspondingly so that in the end all fibrils are oriented as in the cardiac fibers.

Many students of morbid anatomy have described, in the length of the atrio-ventricular bundle, tumors, thromboses, atheromatous alterations, calcareous deposits, gummata or other syphilitic lesions resulting often in alterations not only of the bundle but even of neighboring parts of the myocardium. In this connection reference may be made to the work of Stengel (1905), Aschoff (1906), Barr (1906), Hay and Moore (1906), Jellick, Cooper and Ophüls (1906), Keith and Miller (1906), Keith and Flack (1906), Schmoll (1906), Tawara (1906), Ashton, Norris and Lavenson (1907), Butler (1907), Fahr (1907), Gibson (1907), Vaguez and Esmien (1907), Fahr (1908), Gibson (1908), Heineke, Müller and v. Hösslin (1908), Herxheimer (1908), Löwenstein (1908), Mönckeberg (1908), Saigo (1908), Cohn (1909,

1911), Griffith and Cohn (1910) and others. In the majority of these cases the lesion is accompanied by the formation of more or less abundant connective tissue and even of infiltration by lymphocytes denoting recent or old-standing inflammation which provokes alterations in the muscular portions of the bundle notably their atrophy, necrosis or complete disappearance. Keith and Miller describe a case in which the continuity of the stem of the bundle was completely interrupted in spite of which the Purkinje fibers in the terminal arborization remained intact. Saigo describes an enlargement of the Purkinje fibers from a separation of the myofibrils and a vacuolization of the cell body ending in the disappearance of the transverse striation. Sometimes he has perceived that the vacuolization is accompanied by granular disintegration of the fibrils. At other times the vacuolization, the granular disintegration and the reduction in volume of the fibers are brought about by proliferation of connective tissue, by hemorrhages, by hyaline thrombi or by a proliferation of adipose tissue.

V. PERSONAL INVESTIGATIONS (DESCRIPTIVE)

A. STRUCTURE OF THE ATRIO-VENTRICULAR BUNDLE

If the structure of different segments of the atrio-ventricular bundle be compared, it is apparent that muscular cells of varying appearance exist not only in one part or another but even in the same segment. These differences are due to a gradual and slow evolution of the Purkinje elements which in an adult man, of from 36 to 42 years, attain variable degrees of development. We shall distinguish three successive stages; Purkinje cells which have retained an embryonic appearance, cells of adult aspect, and cells which represent states of transition toward myocardial fibers. Between these three types one encounters every intermediate form.

1. Purkinje Cells of Embryonic Type

These are elements which, having undergone relatively little transformation, recall young or embryonic stages. They are present in greatest number in the normal heart and principally in the ventricular segments (Pieces 11, 8, 5 and 1). Figures 1 and 2 represent them. They are bulky cells, polyhedral or polygonal in section or even prismatic, their longitudinal being a little greater than the transverse diameter.

Towards the center of the protoplasm they show two (np^{II}, Fig. 2), three, four (np^{IV}, Figs. 1 and 2), occasionally five, (np^{V}, Fig. 1) nuclei which are relatively small, oval, of equal size joined together as five or four or even two and two. In the course of evolution they have a tendency to be shifted along the axis or lateral to the axis of the cell body (np^{IV}, Fig. 2).

The cytoplasm is represented by a perinuclear granular zone and a cortical fibrillar area. The central, axial or perinuclear zone is formed by mitochondrial granules arranged in granular filaments or chondriomites (m, Fig. 5), the axis of which is parallel or oblique to that of the cell. Other coarser granules, isolated or heaped together, correspond to pigmentary elements or fatty globules (fg, Figs. 1, 2, 5). All these granules are separated by a paler non-staining substance which in certain preparations is perfectly homogeneous but which in others is formed by a very delicate network, in the meshes of which one sees a pale liquid. This cytoplasmic reticulum is visible along the axial protoplasm in Fig. 5. In the two cells *p* of Fig. 6 it constitutes a very large, clear, periuuclear zone occupying the greater part of the cell body. The mitochondria (m) are quite visible in the neighborhood of the cortical layer: they do not exist at all or are very rare in the clear perinuclear zone which is undoubtedly the perinuclear layer of Schockaert. This clear central zone is equally visible round the two groups of nuclei of the cell np^{IV}, Fig. 2 and of the cell np^{II}, Fig. 1.

In the granular zone one often sees myofibrils isolated or united into very fine bundles. They are transversely striated and make defects in the clear perinuclear zone.

Finally, in certain Purkinje cells of embryonic type there occur in the axis of the cytoplasm one or more bodies of compact appearance and almost homogeneous, staining with Congo red or light green. The significance of these elements we do not know. In transverse sections of the cell these formations resemble an attraction sphere, but in longitudinal sections they often form a kind of axial strand either interrupted or divided into two or three segments (st, Fig. 5).

The cortical or peripheral layer of the cytoplasm is plainly fibrillar. It is formed by dense myofibrils separated by a granular sarcoplasm with abundant mitochondria and is very variable in thickness. Exceedingly thin in the case of cells in Fig. 6 it becomes thicker in Fig. 5, and encroaches upon a great part of the granular zone in the cells of Figs. 1, 2 and 3. Its diameter varies inversely with that of the central zone.

In certain cells, the nuclei of which move laterally from the primitive axis (np^{iv}, Fig. 2; np^{ii}, Fig. 4), the myofibrils differentiate in the axial part of the sarcoplasm and produce a mesial partition which subdivides the cell into two symmetrical or asymmetrical parts. As a result of this singular feature the element originally possessing a single axis gradually acquires a dual character and a tendency to reduplicate itself in two parts, each provided with a nucleated and sarcoplasmic axis. Later, in the Purkinje cells of adult type, this double character becomes more manifest. Further on we shall discuss its true significance. It is quite apparent in the Purkinje cell of embryonic type in Fig. 8, an element of very considerable bulk and almost as broad as it is long. In each lateral half there exists a nucleus np^{i} and np^{ii} and between these two halves there is a septum of myofibrils, the course of which is irregular.

The myofibrils of the cortical layer and those of the granular zone, the latter, however, being much scantier, are generally grouped in bundles which may be described as muscular columns or sarcostyles, the disposition of which is identical with that of the sarcostyles in the Purkinje cells of adult type, a subject of which we shall speak later. These bundles are separated by a great quantity of sarcoplasm which is much more abundant than in the cells of the myocardium. Although each myofibril, seen in its length, shows a transverse striation as characteristic as that of the cardiac fibers, the longitudinal striation is always much more accentuated than is the transverse. Purkinje cells of adult type present a similarly characteristic structure. Fixed by the methods we have employed the myocardial cells always show a transverse striation much better marked than the longitudinal. Between these two elements there exists a very great difference not only in point of size and form, in number of nuclei, quantity of sarcoplasm and of myofibrils but still more in striation. To appreciate the importance of this morphological character one has merely to compare the cardiac fibers with their very obvious transverse striation (Fig. 7) and the Purkinje cells in which the longitudinal striation is predominant (Plate I). By this comparison we may pick out doubtful forms and particularly the stages transitional between Purkinje fibers and true cardiac fibers. At what age this differentiating character appears in the human heart it is impossible at the outset to determine with the precision desirable for the making of an easy diagnosis between the two types of muscular cell.

Whereas in the myocardium the myofibrils present a very regular arrangement, in the atrio-ventricular bundle, and above all in the interior of many Purkinje cells of embryonic type, this arrangement is more variable. In this connection one can distinguish the following forms:

1. Cells with parallel myofibrils. In these the fibrils are parallel more or less with the axis of the cytoplasmic body (Figs. 1, 2, 5).

2. Cells with intercrossing fibrils. The fibrils decussate in two different directions (df, Figs. 3, 4, 8 and 9).

3. Cells with plexiform fibrils. In these the fibrils intercross in many directions so as to form a fibrillar intracytoplasmic plexus (pl, Figs. 9, 11, 12 and 13). The myofibrils of the second and third categories can propagate the contraction wave in two or more different directions and can communicate it to many neighboring cells. This morphological character is of great importance in the conductive function of the atrio-ventricular bundle. An anatomical basis not less important is represented in two other types of elements the first of which we shall designate by the name intercalated or association-cells and the second, constituted by a group of cells arranged in plexus form, we shall term the cellular network of Purkinje.

4. Intercalated or association cells are interposed either between two longitudinal bundles of Purkinje fibers the axis of which is parallel to that of the atrio-ventricular bundle, or between a longitudinal bundle of Purkinje fibers and a longitudinal bundle of cardiac fibers. They are irregularly polyhedral elements (p and pl, Fig. 11) or cells a little longer than broad (np, Fig. 10; p, Fig. 13). They correspond therefore to Purkinje cells of embryonic type. Their axis is directed at right angles or slightly obliquely to that of the neighboring longitudinal bundles. Some, the simplest ones, possess parallel myofibrils (Fig. 10), others intercrossing or plexiform fibrils (Figs. 11, 13 and 15). But all these fibrils pass uninterruptedly into the cytoplasm of the two longitudinal cells which they connect and in the interior of which they become continuous with the longitudinal fibrils (con, Fig. 10). In the arrangement and the relations of their constituent parts these elements recall somewhat the association neurones in the central nervous system itself which transmit the nervous impulse between different elements of the cerebro-spinal system.

5. The cellular networks of Purkinje are formed by three or more short cells anastomosing to form a network in the spaces of which

there is a vascular connective tissue. It may be that intercalated discs delimit their apposed ends (id, Fig. 12) or sometimes these discs are absent and in that case the network is a real syncytium. In both cases the myofibrils (pl, Fig. 12) decussate in many cellular areas and continue without interruption across the different trabeculæ of the network. These plexuses are very numerous throughout the atrio-ventricular tract in the adult man (see tabular summary). But in the trabecular tissue of the left ventricle (Piece No. 10) of the normal heart one perceives still more complicated appearances, namely, stellate plexiform formations (Fig. 14). Many Purkinje cells embryonic in type, short and broad, are arranged radially about a central plexiform cell (pl). The myofibrils which are arranged almost uniformly in the peripheral cells penetrate into and decussate within the central element whence they continue into the peripheral cells of the opposite side. There exists no demarcation between the central element (pl) and the peripheral cells in this stellate formation.

In his description of the atrio-ventricular bundle in the sheep, in the dog and in man, Tawara (1906) emphasizes the presence of reticular and plexiform appearances. In the heart of the sheep he describes in the atrial portion of the bundle an "ausserordenlich complizierte Netwerk" with very slender fibers, much more slender indeed than those of the neighboring myocardium and of very variable length. The same fiber is in some parts bulky and in others more slender. The myofibrils are less developed than in cardiac fibers and they produce a longitudinal striation, irregular rather than parallel, and a transverse striation which is only slightly apparent. In the spaces of the network one finds fatty tissue with small vessels and nerves. Often four or six fibers bound together produce a stellate formation around a central thick node where the fibrils decussate in all directions.

In the ventricular part of the bundle which commences where the bundle pierces the fibro-cartilaginous atrio-ventricular septum Tawara distinguishes an initial portion (Anfangstheil) and terminal expansions (Endausbreitungen). In the initial portion the bulky muscular cells are united into strands bound together to form a very irregular network, and their fibrils, more numerous than in the terminal expansion, are more or less parallel with the axis of the strand. The coarse fibers of this proximal ventricular segment resemble Purkinje fibers of the terminal portion with which indeed they are continuous, but there are certain quite distinctive features.

In the dog the bundle is formed by elements which are not so definitely distinguishable from myocardial fibers as in the sheep. The atrial part includes an anterior reticular part and a posterior portion with parallel fibers. In the former the fibers compose a close meshwork indistinctly striated transversely with abundant cytoplasm and relatively few myofibrils. They contain isolated nuclei, less frequently two neighboring nuclei and very occasionally even three closely related nuclei. The muscular fibers are in general finer than those of the myocardium but thicker than in the corresponding segment of the sheep's heart. The spaces of the meshwork also are smaller. This network constitutes a node (Knoten) the fibers of which are continuous with the parallel and very slender fibers of the posterior atrial portion. In the latter the longitudinal and transverse striation is less pronounced and the nuclei are more numerous than in myocardial fibers. At the beginning of the first ventricular segment, namely the stem, Tawara finds the same appearances as in the " Knoten," but the meshwork is less complicated and the fibers become more parallel. As in the Knoten the myofibrils run in an irregular course but they are less frequent and more delicate than in the cardiac fibers. They produce a network in the abundant protoplasm. Their course becomes more regular after the trunk has divided up into its two branches.

Tawara summarizes in the following terms his description of the terminal expansions of the atrio-ventricular bundle of the dog (p. 146), " Die Muskelfasern dieses Systems sind fast immer mit einer bindgewebigen Scheide versehen, die viel stärker als das Perimysium der Herzmuskulatur ist . . . . Diese Muskelfasern sind meist aus zahlreichen, hintereinander liegenden, relativ kurzen und breiten Sarkoplasmaterritorien zusammengesetzt und zeigen deshalb in gewissen Abstände sehr deutliche Grenzzonen, während man in den gewöhnlichen Herzmuskelfasern des Hundes wohl Kontraktionslinien, aber keine Grenzzonen finden kann. Als weiteren Unterschied muss man die relativ geringe Zahl und den unregelmässigen Verlauf der Fibrillen und das demgemäss reichlich vorhandene Sarcoplasma der Fasern der Endausbreitungen des Bündels aufzählen. Endlich ist die oben zuletzt erwähnte, höchst komplizierte Fibrillenordnung an den Knotenpunkten der verschiedenen Endausbreitungen so eigenthümlich, dass man ein solches Bild niemals in der gewöhnlichen Herzmuskulatur sehen kann."

Finally, he describes an appearance peculiar to the heart of the dog and found at the level of the terminal ventricular segment where a muscular bundle divides into two or three twigs or where several bundles joining together produce a nodal point (*Knotenpunkt*). At this site, says he, the muscular bundles and the muscular fibers frequently resolve themselves into many small fibrillar groups and partly even into isolated fibrils like the spread out fingers of the hand. These become bound together with other muscular fibers and thus produce a very complex network. (See Tawara's Fig. 10, Plate IV.)

Tawara's description of the human heart is brief. In structure the atrio-ventricular bundle resembles that of the dog. In the atrial part the fibers, which are very slender, form the usual network but the spaces in this are larger. The first part of the ventricular segment presents parallel fibers alone. In the terminal expansions the muscular fibers appear to contain more fibrils than in the dog and for this reason they resemble cardiac fibers more closely. Tawara then draws attention to certain pathological details.

The foregoing summary of the results obtained by Tawara, in great part confirmed in the human heart by Mönckeberg (1908), shows that the former author attributes great importance to the plexiform or retiform arrangement of the constituent parts of the atrio-ventricular bundle. De Witt (1909) adopts the same attitude. In studying the *node* in the sheep, the cow, the dog, the cat and man, he states that the anastomosis of fibers occurs "not by simple fusion of two united branches, as is usual in heart muscle, but by the formation of nodes or star-like forms, into which two or three, or more, fibers become merged and from which a variable number of fibers emerge. In the *node* the fibers completely lose their identity, fibrils from the different fibers commingling confusedly" (p. 491). These fibers are less bulky than the cardiac elements of the atrium. Later in describing the Purkinje fibers of the terminal expansions in the dog, in the cat and in man, De Witt states: "The fibers are very variable in size and nodal points showing a commingling of fibrils from different fibers are frequent." These plexiform appearances are very similar to the features of the Purkinje cells of embryonic type in the human heart described by us above. It is important to observe, however, that in our material these special structures do not present in any segment, even in the atrial node, so marked a generalized character as appears from Tawara's account. From this point of view our Fig. 44 undoubtedly

accords most closely with Tawara's description. It is reproduced at a magnification of 45 diameters and shows a transverse section of the first part of the trunk or perhaps the inferior part of Tawara's Node (Piece 5) in the pathological heart. The muscular elements are represented by Purkinje cells of adult type of which about a third are of medium transverse diameter and a little thicker than those of the neighboring myocardium, while the others (two-thirds of the whole) are very fine and more slender than the cardiac cells. The majority of the bundles or groups of fibers (gr) present a regular disposition parallel with the axis of the atrio-ventricular bundles; some others are arranged obliquely or even in circular fashion relative to this axis and show a tendency to anastomose to form a network. In Fig. 43 which represents a transverse section of the septal wall of the right atrium in the normal heart (Piece 7) the Purkinje fibers of adult type (lp) are of medium diameter: they are a little larger than those of the neighboring myocardium (lc) and are arranged throughout very regularly. But in sections of the same piece (Piece 7) cut tangentially to the surface of the endocardium one observes certain reticular formations not more numerous here, however, than in other segments of the atrio-ventricular bundle. In other atrial portions lying near the orifice of the superior vena cava (Pieces 15 and 16; Figs. 47 and 48), and near the coronary sinus (Pieces 6 and 14; Fig. 51) the Purkinje fibers of adult type are in general of medium thickness or even slender, the former being much thicker than those of the neighboring myocardium. In the trunk (Piece 5) of the normal heart they are thick and also in the two branches (Pieces 4 and 8), although in the left branch (Piece 8) there may be some slender ones and others of medium thickness. In all these segments as in the terminal expansions one can see reticular formations produced by the Purkinje cells of embryonic type, but the great mass of fibers shows in general a parallel arrangement similar to that of the cardiac fibers. These appearances are specially well marked in sections cut tangentially to the endocardial surface.

We may therefore sum up by saying that the Purkinje fibers of the atrio-ventricular bundle in the adult man present in general a regular arrangement, but that in most segments one encounters bulky cells which are of embryonic type, short and polyhedral or a little longer than broad. Some possess myofibrils parallel with the axis of the cytoplasmic body; others exhibit myofibrils decussating in two or more directions and others again group themselves in such a manner as to

produce a plexiform cellular network and occasionally stellate formations. All these features like the intercalated cells give an anatomical basis most favorable for the transmission of the contraction wave in various directions.

In general the Purkinje cells of embryonic type exhibit a very precise delimitation. The polyhedral elements show along some of their surfaces a fine connective tissue, often vascular, a sort of endomysium which separates them from neighboring cells (enm, Figs. 1, 2, 3 and 4). Other surfaces of the polyhedron are delimited from the cytoplasm of adjacent elements by actual intercalated discs (id) absolutely identical with those visible in the length of the cardiac fibers (id, Fig. 7). They are traversed by the myofibrils which are continuous over several cellular areas. Those cells, which are a little longer than broad, exhibit a connecting septum of endomysium on their lateral surfaces (enm, Figs. 8, 9 and 12) and intercalated discs (id) separating their extremities. A photograph does not bring out satisfactorily the difference in appearance between the septa of connective-tissue (enm) and the transverse discs (id), but in the preparations it is easy to distinguish between them. Stained by Mallory's method the former are colored blue and the second red; in preparations stained with safranin and light green the septa are green and the discs red.

This well-marked delimitation of cellular contour is lacking at the extremities of the intercalated cells (Figs. 10, 11, 13 and 15) and at the extremities of certain plexiform figures such as that in Fig. 14.

2. Purkinje Cells of Adult Type

These are elements elongated, cylindrical or, as a result of reciprocal pressure, prismatic or even flattened and, in this case, they are laminated and elongated in transverse section. Often they correspond to half or a third of a cylinder or prism and in such cases they show, on transverse section, a plane surface adjoining the similar surfaces of neighboring cells and thus giving a tessellated appearance (Figs. 21, 22, and 23). This arrangement recalls the appearance resulting from the grouping of cartilage cells three or four together. We shall show that here, as in cartilage, this appearance may be produced by the division of a mother-cell into two, three or four daughter elements.

They form the great mass of the Purkinje fibers in the whole extent of the atrio-ventricular bundle, but they vary in thickness from one

segment to another (see tabular summary). The majority of these elements in the normal heart should be considered as multinuclear cells, real polykaryocytes (Howell). These nuclei are generally equal in size and a little larger than those of the cells of embryonic type; but one sometimes encounters nuclei of very considerable bulk (np, Figs. 24, 33 and 37). The nuclei are rounded or oval and in their morphological characters they more closely resemble the nuclei of the true cardiac elements (nca, Fig. 7) as the cell is more evolved and hence more closely approaches in appearance the cells of the myocardium (Fig. 42). In very rare instances only are all these nuclei noted in a single longitudinal section so that it is difficult to determine their exact number. Especially is this difficult since the nuclei are shifted and may lie quite distant the one from the other. This shifting, active or produced by an extension of intermediary cytoplasma and already indicated in the case of the cells of embryonic type, becomes gradually more marked in both lateral and longitudinal directions. It seems to have attained its extreme limits in Fig. 18. This represents a bulky single cell which we shall call a mother-cell (pm); it is almost isolated on the section in the midst of an abundant vascular connective tissue (v). This last is brilliantly stained with light green, whereas the cell is colored red. Except for a fine green septum (enm) which penetrates a short distance into the extremity of the cell body no trace of division of the protoplasm is visible. This cell encloses five nuclei labeled respectively np^{I}, np^{II}, np^{III}, np^{IV} and np^{V}. Two are situated at one pole of the protoplasm and three at the other. Figs. 17 and 19 show different stages of this gradual shifting of nuclei. In the former one notes to the right a bulky cell although shorter than that in Fig. 18. It encloses two nuclei np^{I}, np^{II}, separated in the axial direction. To the left another cell shows two nuclei np^{I}, np^{II}, withdrawing themselves in the lateral direction and separated by a septum of myofibrils. Fig. 19 shows a mother-cell (pm), in one half of which there is a group of two nuclei (np^{I-II}) and a third (np^{III}) situated a short distance from the others. Figs. 17, 18 and 19 show us, then, stages in growth and elongation of the Purkinje cell accompanied by a removal of the multiple nuclei both laterally and longitudinally.

The cytoplasm is represented by sarcoplasm and myofibrils. The abundance of the former varies inversely with the number of the latter. The sarcoplasm is a pale reticulated substance strewn throughout with mitochondrial (m, Fig. 20), fatty and also pigmentary granules. The

enigmatic axial strand described in Fig. 5 (st) persists in the cells of adult type (st, Fig. 23). In the embryonic type of cell the sarcoplasm produces a perinuclear zone of rounded form or tapering in the axial direction. In elements of adult type it occurs as an axial band in "unipartite" cells (Figs. 17 and 20), as two lateral bands in "bipartite" mother-cells (Fig. 17, left side; pm, Fig. 19) or as three bands in the "tripartite" cells (Fig. 18). The multiple nuclei are distributed in these sarcoplasmic bands, to the opposite poles of which they draw with the advancing evolution of the cell. The bipartite or tripartite cells are often asymmetrical.

At the beginning of these transformations myofibrils are rare in the sarcoplasmic zone, but they become gradually more numerous in definite directions of the large mother-cells. In this manner they produce in the bipartite elements a myofibrillar partition and in the tripartite elements two apparent partitions subdividing the cell body into two (Fig. 19) or three portions (Fig. 17, cell to the left enclosing two nuclei np^{I}, np^{II}). Each part or lobe encloses one or two nuclei. These partitions, as transverse sections show, are often in direct relation with the cortical myofibrillar layer (pt^{II}, Fig. 23) which gradually extends between the two halves of the cell.

In general the Purkinje cells of adult type possess a peripheral cortical layer, the myofibrils of which are much more numerous than those of the axial sarcoplasmic zone. Longitudinal sections show this feature, but it is especially obvious in transverse sections. This is confirmed in the normal heart by Figs. 21 and 22 and in the pathological organ by Figs. 23, 24, 25 and others. But these same photographs also show many cells, the central parts of which are strewn with a large number of myofibrils to such a degree that one can see no delimitation between their two zones. This observation applies to certain Purkinje cells of embryonic type (Figs. 3, 4 and 12) and especially to the Purkinje fibers of adult type in the stem and atrial segments of the bundle (Figs. 22 and 47). This more or less uniform distribution of myofibrils across the whole thickness of the cell body is undoubtedly the morphological character which most strikingly distinguishes the Purkinje cells of the atrium from those of the ventricles. Furthermore, the cells of the ventricle are in general thicker. It is important to observe, however, that in the atrium one may note bulky elements and cells with a quite distinct central sarcoplasmic layer, whereas in the ventricular segments one observes

slender cells and elements with myofibrils uniformly distributed in the whole thickness of the cytoplasm. Differences in volume and in distribution of myofibrils are merely secondary accessory features, which depend upon the stage of evolution in a single type of cell. For this reason we shall consider the muscular elements of all segments of the atrio-ventricular bundle as belonging to a single type—the Purkinje cell. The fundamental character by which one easily distinguishes Purkinje cells of either atrium or ventricle from cardiac elements is the constant presence in much greater abundance of an interfibrillar or inter-fascicular sarcoplasm. This feature gives to the Purkinje cells a quite distinctive, clearer and less compact appearance. The fibers of the myocardium are more deeply stained and are denser. This difference in morphological appearance is visible in all our photographs, even in those reproduced at a low magnification. It can be seen in the ventricular segments (lp and lc, Figs. 26 and 27), the stem (gr, Fig. 44) and its branches (rbr and lc, Fig. 46), in the atrial segments (lp and lc, Figs. 43 and 48) and even where the Purkinje fibers are intermingled with myocardial bundles (lp and lc, Fig. 51). Keith and Flack (1906), among others, have already drawn attention to this difference in appearance and insist upon its physiological importance, it being accepted that pale muscles contract more rapidly than red muscles. We would add that the great abundance of sarcoplasm, together with the presence of a smaller number of myofibrils in the Purkinje elements, constitutes a second distinctive and not less important morphological feature, which relates to the nature of the striation. The longitudinal striation is more pronounced than the transverse in the Purkinje cells, whereas the transverse striation preponderates in the cardiac elements.

Grouping of myofibrils in columns. It is known that the myofibrils of cardiac cells and even of Purkinje cells tend to unite in the midst of the cytoplasm into muscular columns or sarcostyles, between which there exists a sarcoplasm more abundant than between the fibrils of the columns themselves. This arrangement is well marked in all Purkinje cells in the adult man, but the form of the sarcostyle is exceedingly variable from cell to cell and even within a single cell. Columns can be distinguished presenting the form of prisms, rods, or again of hollow cylinders. The prismatic and rod-like columns are made up of a compact bundle of myofibrils, whereas the hollow cylinders are formed by a peripheral myofibrillar sheath surrounding a sarcoplasmic axial por-

tion (Fig. 21, the large cell p). Other columns are laminated and generally occur in the cortical layer of the cell (Fig. 21). In transverse sections they are visible as thick striæ arranged radially in relation to the central sarcoplasm. The striæ may be simple and thick, or double and formed by two fine parallel streaks separated or united in part of their course. This feature seems indeed to indicate a cleavage into two of one primitively single lamella. All these types of columns are found in the pathological heart just as in the normal organ, but in the former their arrangement is much more variable and complicated and often it is related to longitudinal cleavage of the Purkinje cells.

3. Longitudinal Segmentation or Cleavage of Purkinje Cells

M. Heidenhain (1902) has described a process of longitudinal division in myocardial fibers—the segmentation of "mother fibers" into "daughter fibers." This occurs through the appearance of a system of longitudinal clefts which delimit a myofibrillar bundle in relation to a segment of the intercalated disc. These clefts, which are very narrow, are occupied by a clear substance from which all trace of transverse striation is obliterated and in which there appears a simple sarcolemma-like membrane in continuity with the discs Z of neighboring myofibrils. This membrane, which is at first single, doubles itself later into two, the "two daughter sarcolemmata" adherent to the surface of the "daughter fibers." Heidenhain studied this process in sections parallel with the axis of the cardiac fibers, but he does not speak of the appearance seen in transverse sections.

The longitudinal cleavage of Purkinje cells should be studied in transverse as well as in longitudinal sections. It is indeed more marked and better visible in the pathological heart than in the normal organ, but it exists in both throughout the length of the atrio-ventricular bundle.

In transverse sections are seen the three types of cells described above.

1. Cells with a cortical myofibrillar layer and a central sarcoplasmic zone.

2. Cells in which the myofibrils are more or less regularly distributed throughout the whole extent of the cytoplasm.

3. Cells of the subdivided type, bipartite or tripartite. This last really represents the first stage preparatory to longitudinal cleavage. One or two myofibrillar partitions subdivide the mother-cell into two

(pt^{II}, Figs. 21, 23 and 30) or more lobes, more or less symmetrical in size and in structure. At other times, and especially in the pathological heart, these lobes are asymmetrical, in that one half of the protoplasm, closely resembling the cytoplasm of a cardiac cell, contains many more myofibrils than the other half. In Fig. 29 there is a cell (asp) of which the lateral half is clear and the other half very darkly stained. This cell is obviously asymmetrical. The same is true of a mother-cell in Fig. 25 in which an arrangement of partitions (pt^{III}) divides the cell into three parts, one very rich in myofibrils (pc) and two others which differ in size, one of which contains a nucleus (np). In Fig. 24 a partition (pt^{IV}) subdivides the mother-cell into four slightly asymmetrical segments, while the partition pt^{III} divides another cell into three symmetrical segments. In the pathological heart one observes not infrequently the differentiation of the axial cytoplasm to resemble that of a cardiac cell. It is deeply stained (cc, Fig. 23) and distinctly marked off from the peripheral zone, which retains the primitive features characteristic of the Purkinje cell.

In the second stage of cleavage the endomysium surrounding the mother-cell proliferates into the intracytoplasmic myofibrillar partition and subdivides the cell body into two symmetrical daughter-cells (p^{II}, Figs. 22, 25 and 28; pc^{II}, Figs. 22 and 29), into two asymmetrical daughter-cells (asp^{II}, Figs. 23 and 28) or even into three or more asymmetrical elements (asp^{III}, Figs. 22 and 23). Special attention should be given to two bulky mother-cells which are absolutely pathological. The one (pm, Fig. 28) shows the commencement of cleavage into five lobes of very different size by fine partitions of endomysium (enm) in continuity with the thick pericellular endomysium. The other (pm, Fig. 30) has undergone an apparently irregular cleavage in its lateral half.

These intracellular connective-tissue septa originate undoubtedly from an extension of the neighboring endomysium. At the beginning they are thin, but in the pathological heart they may become thick and, when the daughter-cells are completely separated, they may attain a considerable thickness which is characteristic of the following stage.

In the third stage of cleavage, limited exclusively to the pathological heart, the daughter-cells, two or three in number, are separated by a thick connective-tissue partition and even a former cleavage of the mother-cell can be recognized owing to the regularity of the old method of segmentation represented in transverse section by a straight line.

In other words, the cylindrical mother-cell has been subdivided into two half cylinders of which the plane surface of cleavage remains recognizable and characteristic (p^{II}, Fig. 24) and is formed by a thick partition of endomysium. These figures irresistibly recall the similar appearances characteristic of groups of two or four cartilaginous daughter-cells resulting from the mitotic subdivision of a maternal element.

Finally, in a fourth stage, namely that of atrophy of the Purkinje fibers in the pathological heart, the twin cells in their turn undergo a repeated longitudinal cleavage, which induces reduction in their size and later atrophy. One of the two daughter-cells (p^{II}, Fig. 24), which are separated by a thick intercellular partition, shows a tripartite condition (pt^{III}), owing to cytoplasmic differentiation of two thick myofibrillar partitions. A similar differentiation (pt^{III}) may be observed in one of the two daughter-cells (p^{II} in Fig. 25). These appearances indicate that twin cells undergo a longitudinal cleavage in their turn. In several regions of the ventricular parts of the atrio-ventricular bundle one finds Purkinje elements much reduced in size as symmetrical (ap^{II}, Figs. 29, 32 and 34; ap^{III}, Fig. 34) or asymmetrical ($asp^{II}a$, $asp^{III}a$, Fig. 32) daughter-cells. These twin elements represent stages in the atrophy which we believe are provoked especially by this process of repeated cleavage. Their transverse diameter scarcely surpasses that of a smooth muscular fiber. Often this atrophy is accompanied by the appearance of a plainly visible internal cytoplasmic membrane. This, differentiated in the midst and at the expense of the protoplasm, separates a clear perinuclear protoplasmic zone free from myofibrils from a fibrillar cortical layer (im, Figs. 32 and 34) of which the sarcostyles or the isolated fibrils always show a transverse striation.

This process may be still more accentuated, the atrophied cells in their turn undergoing a cleavage into smaller elements (ap, Figs. 32 and 34) either isolated or grouped together and representing the last vestiges of Purkinje fibers. In extreme atrophy these vestiges are simply small cytoplasmic masses which may or may not be nucleated and possess a few occasional myofibrils. But from the point of view of function of the atrio-ventricular bundle the majority should be considered as completely devoid of contractility and of the power to conduct the contraction wave.

In order to obtain an exact idea of this atrophic process of the Purkinje elements in the ventricular part of the pathological heart, one

ought to examine not only Figs. 32 and 34, the fibers in which are atrophied, but also Fig. 21 in which the fibers are normal. All three are magnified 476 diameters. In this comparison should be included Figs. 26 and 27 reproduced at a magnification of 85 diameters. The first is a photograph from Piece 10 of the normal heart and the second of Piece 9 of the pathological organ. Fig. 26 shows throughout the whole extent of the Purkinje layer (lp) bulky cells of a uniform diameter, whereas Fig. 27 shows, beside many bulky cells (p), others of medium size and a multitude of others very small and atrophied (ap). Many of these last appear as small clear spots the size of which does not surpass that of one of the lymphocytes which infiltrate the neighboring inflamed interstitial tissue (cti) in large numbers.

Longitudinal sections parallel to the axis of the Purkinje cells show equally plainly different stages of their cleavage in length. These figures are undoubtedly less clear than those seen in transverse sections. They must be analysed, however, to enable us to study the process of proliferation in the septa of the endomysium throughout the entire length of the cytoplasm, and the distribution of the multiple nuclei of the mother-cell in the interior of the daughter-cells.

A first series of figures (Figs. 18 and 17) shows us the arrangement of partitions in a tripartite mother-cell, the former with the nuclei distributed at the poles of the future daughter-cells, the latter with an arrangement of two septa of myofibrils (pt^{III}) subdividing the cytoplasm into three parts. A second series of figures (Figs. 20, 19 and 31) gives us an exact idea of the extension of the endomysial membrane throughout the length of the mother-cell. Fig. 20 shows an element of which one extremity is subdivided into two unequal portions by a septum (enm). In Fig. 19 the septum attains the level of the two cohering nuclei (np^{I-II}); and in Fig. 31 the endomysium (enm) which possesses a blood vessel (cp) divides the mother-cell (pm) almost completely into two equal halves of which the one possesses a simple nucleus (np^{I}) and the other two (np^{II}, np^{III}) a single one at each pole of the future daughter-cell. The arrangement of the nuclei before any trace of cleavage (Fig. 18) and before the completion of longitudinal division (Fig. 31) tends to show that each twin cell encloses two or three nuclei distributed generally at the two cytoplasmic poles.

When segmentation is completed it is difficult, usually impossible indeed, to recognize in longitudinal sections the twin cells produced by the cleavage process. The preparations of the pathological heart,

however, furnish us invariably with another series of figures (Figs. 35 and 36) in which one can recognize a characteristic grouping into two or three daughter-cells. An abundant connective tissue separates the groups one from another; a fine septum of endomysium separates the twin elements from each other within a single group. In Fig. 35 the majority of the daughter-elements are represented by one bulky cell and by another much smaller (p^{II}). In Fig. 36 the interstitial connective-tissue separating the groups is infiltrated by a great number of leucocytes (cti), but the septa of endomysium between the constituent parts of a single group are in general lacking altogether in these inflammatory cells (p^{II}). In this illustration one sees, furthermore, a mother-cell (pm) very bulky and segmented at one of its extremities, besides other groups each of two twin elements (p^{II}), the total transverse diameter of both elements being almost equal to that of the mother-cell.

The longitudinal cleavage of the Purkinje cells in the pathological heart may be accompanied by segmentation phenomena or direct division of the nuclei induced by extension of the proliferating connective-tissue septum. Fig. 24 shows a nucleus (np in the upper part of the figure) formed by two unequal lobes united by a constricted portion. At the opposite side of the illustration (np, in the lower part of the figure) there is visible a nucleus equally lobulated abutting upon a septum of endomysium (enm) which appears to have brought about this irregular form of the nucleus. Longitudinal sections parallel with the axis of the Purkinje cell show appearances more convincing for a decision as to the causative relation of the proliferating connective-tissue to nuclear segmentation. In Fig. 33 one observes a mother-cell partially subdivided into two daughter-elements (p^{II}) by a median septum (enm) of endomysium, pale in the photograph but colored blue in the preparation which is stained by Mallory's method. This septum indents the bulky nucleus (np), thus forming two lateral nuclear lobes, one lobe for each future daughter-cell. In Fig. 37 the nucleus (np) has been almost entirely pinched into two halves by the septum (enm), which though pale in the photograph is clearly stained blue in the preparation. It separates also in part the mother-cell into two twin cells, p^{I} and p^{II}. These two last figures leave no doubt as to the influence of the invading connective-tissue upon the process of amitotic division of the mother-nucleus.

We have already noted the presence of blood capillaries in the interior of endomysial septa which provoke the cleavage of mother-cells (cp, Fig. 31). Fig. 38 shows another example of this in the atrial segment (Piece 6) of the pathological heart. In this may be seen an element with a rounded nucleus (np) surrounded by a clear granular sarcoplasm with numerous pigmentary granules (pig). It is partly subdivided into two (p^{I}, p^{II}) by a connective-tissue septum (enm) stained green in the preparation. This septum reaches the perinuclear sarcoplasmic region and contains as far as its most advanced point a blood capillary (cp) in which are visible the central lumen and the endothelial wall in which there is a nucleus. This figure shows that the septum of cleavage not only can include capillaries but even that the capillary precedes and appears to direct the connective-tissue in its invasion of the cell. The phenomenon is comparable to that observed in the vascular osteogenic buds which penetrate into the centers of ossification of a bone at the time of resorption of the calcified cartilage.

All the figures described so far tend to prove that the vascular endomysium invading the cytoplasm of a mother-cell occurs as a septum dividing into two parts the extremity of the cytoplasm. Fig. 39 shows a Purkinje cell cut transversely at the level of one of its nuclei (np). At the center of the sarcoplasm is seen a blood capillary (cp) filled with red corpuscles (rc) quite comparable with those shown in a neighboring capillary (rc). This figure proves that the invading tissue may sometimes assume the form not of a septum but of a rounded cord or at least a kind of vascularized papilla following the axis of the cylindrical cell. Jordan and Banks (1917) draw attention to a similar feature in their Fig. 42 where "an artery appears to be within the cell. This definitive condition is probably the result of a secondary adaptation of the cell to the growing bloodvessel" (p. 305). From the above description it follows that the Purkinje cells of the normal heart possess quite a special morphology. No other tissue shows stages so varied as regards the distribution of the nuclei, the transformation from a unipartite element into a bipartite or multipartite element, or the consequent division of the cell body. These stages really represent a series of successive phases which terminate in the longitudinal cleavage of a mother-cell into smaller and simpler daughter-cells. The subdivision is provoked or at least accompanied by a proliferation and extension of the neighboring vascular perimysium.

In the pathological heart the cleavage process is much more pronounced than in the normal organ. It becomes pathological undoubt-

edly under the influence of the etiologic factor syphilis which has induced hypertrophy and sclerosis of interstitial connective-tissue in the atrio-ventricular bundle. This supporting tissue, developed abnormally, exercises an abnormal influence on the evolution of neighboring muscular elements. Many Purkinje cells preserve a normal appearance, but others undergo an exaggerated cleavage more or less pathological, whereas others again divide and subdivide until they are reduced to the condition of atrophic cells in process of complete disappearance. These pathological conditions of atrophy and sclerosis are brought about by two factors occurring certainly in the normal heart but of exaggerated activity in syphilis—the cleavage of the Purkinje cells and the proliferation of the supporting substratum or vascular connective tissue. The Purkinje cells already reduced in size by repeated division are subjected to the detrimental influence of the hypertrophied interstitial tissue. This constricts them, hastens their atrophy and in certain places provokes their complete disappearance. We shall return later to this question.

It is very important from the biological standpoint to know if the division of the Purkinje cells should be interpreted as mitotic or amitotic. We are not able to solve this problem, for it would need to be studied in large part upon embryonic material. The multiple nuclei described in these elements are already formed before or shortly after birth. To solve adequately the problem just stated it would be necessary to know how these nuclei are produced. It is doubtful whether they appear as the result of an indirect division or of a direct division. In the case of myocardial fibers Tangl (1889), Hoyer (1899), Schockaert (1909) and others have observed figures of mitotic nuclear division in the foetus, and they estimate that at some little time after birth the multiple nuclei of the cardiac cells originate by mitosis. Hoyer denies the direct nuclear division described by Solger (1891) and in 1900 the latter author was obliged to admit that the multiple nuclei are derived in part by indirect division and in part by direct division. Marie Werner (1910) has counted in the cardiac cells of various mammals multiple nuclei up to the number of 32 in a cell from the left ventricle of the pig, and she can find no trace whatsoever of mitotic division. Schockaert describes in detail the stages of mitotic division in the cardiac elements and proves that these behave exactly like uninucleated cells. In the anaphase and in the telophase there occurs between the two daughter-cells a cytoplasmic segmentation marked constantly by the presence of an intermediate corpuscle. In the last

stages myofibrils appear prolonged from one cell into another. The cardiac fibers behave, therefore, in these stages of their development not like a syncytial mass but like uninuclear elements.

If the multiple nuclei of the Purkinje cells are produced as the result of a mitotic process, the longitudinal cleavage described above ought to be considered as a final stage in the indirect cell division occurring in the adult man many years after the nuclear mitosis. A similar tardy cleavage has been described in megakaryocytes of the hemapoietic organs in mammals. Van Bambeke and Van der Stricht (1891) have shown that such giant cells acquire a considerable size in consequence of many repeated multipolar mitoses. Their lobulated nucleus is really constituted therefore by a large number of small daughter-nuclei which fuse during the telophase. But this cell, very important from the physiological point of view, is capable of multiplying, of producing two daughter-megakaryocytes. The division of the mother-cytoplasm is always long retarded; it does not take place until after many repeated multipolar divisions of the maternal nucleus. Finally, when the giant nucleus has attained considerable size, it is broken into two by the appearance of a cellular plaque subdividing the giant mother-cell into two daughter-megakaryocytes. This type of direct division is really the complement of the multimitosis and cannot be regarded as an amitosis.

Our knowledge is very limited regarding the formation of multiple nuclei in the Purkinje cells and the division of these elements. Marceau has been unable to find in their cytoplasm nuclei in process of mitosis, but he describes progressive stages of amitotic division. He concludes with the statement: " Les noyaux des cellules de Purkinje ne se multiplient probablement que par étranglement ou bourgeonnement, suivi de scission " (p. 25), and he adds later, " Cependant, la division du noyau peut être suivie elle-même de la division de la cellule, car j'ai observé des cellules en forme de huit de chiffre renfermant un noyau dans chacune des deux boucles alors que dans la région rétrécie on voyait de très fines fibrilles en voie de développement et destinées à compléter l'écorce des deux cellules-filles ainsi formées. Donc chez l'adulte les cellules de Purkinje conservent certainement la faculté de se diviser " (p. 25). On page 61 he expresses himself in the following terms: " Au moment de la naissance le nombre de fibres cardiaques est à peu près atteint et celles qui existent alors ne font que s'accroître et acquérir leur structure définitive. A la même époque les fibres de

Purkinje sont plus grêles et comprennent en épaisseur moins de cellules que chez l'adulte, ce qui montre que pour arriver à leur complet développement les fibres de Purkinje des jeunes animaur doivent être le siège d'une multiplication cellulaire, multiplication qui se continue même chez l'adulte ainsi que je l'ai observé."

In speaking of the structure of the "atrioventricular connecting bundle" Jordan and Banks (1917) find that the nuclei, "arise chiefly by amitotic division of a single nucleus of the original cell, a process which can be observed in fetal hearts of from two to four months. A few nuclei were observed in the segmented spireme condition in the two-month fetal heart, which would seem to indicate that mitotic division may also occur in the earlier stages. In this respect the bundle simply agrees with ordinary myocardium, where nuclear division is originally mitotic and subsequently becomes exclusively amitotic. The tri- and quadri-nucleated condition of the bundle cells follows a later similar amitotic event" (p. 304). Later they state (p. 313), "The cell of the atrio-ventricular bundle is short and very stout, the cells of the Purkinje fibers are longer and less stout, that of the myocardium is still longer and relatively slender. Moreover, each type multiplies its nuclei by amitotic division. The atrio-ventricular bundle cell more generally has only two nuclei; and an occasional nucleus may be seen in amitotic division. . . . The Purkinje fibers progress to a somewhat later stage characterized by an elongated fusiform shape, amitotic division of nucleus, and a fusion to form fibers, the fusion involving the formation of discs."

4. Delimitation of Purkinje Cells of Adult Type

The delimitation is brought about by structures very variously named. Among the terms used we may note intercalated discs, cement lines, intersegmental or intercellular septa, junctional lines, step-like lines. We have already seen that cells of embryonic type are generally isolated laterally by an endomysial membrane and are placed end to end although separated from each other by an intercalated disc. This disc is always traversed by myofibrils continuous from one cell into the other. Precisely the same arrangement is found in the case of the elements of adult type which are much longer than broad. Figs. 16, 17, 19 and 31 show this endomysium (enm) and the junctional lines (id). Even in Fig. 40 reproduced at a magnification of 103 diameters one can see a precise delimitation of all the elements which are oriented

in very different directions. On account of this precise delimitation the Purkinje fibers, formed by the juxtaposition of cells, resemble fibers of the myocardium in which, however, the vascular interstitial connective tissue is much more abundant. If at first sight the lateral contours of the Purkinje fibers are less distinct, it is because the interstitial tissue between them is more reduced and many cells are found in stages of longitudinal cleavage.

From the point of view of structure the intercalated discs, examined in sections parallel with the axis of the fibers, generally appear as transverse lines staining deeply in coloring reagents. The disc appears striated (id, Fig. 31) each stria corresponding to a thickening or more deeply colored disc of a myofibril which, according to the majority of authors, is continuous across the junctional line. Not infrequently one sees double intercalated discs formed from two parallel bands united by finer fibers to form species of intercellular bridges.

Figures of this type clearly prove that the discs are formed essentially by segments of myofibrils more or less modified in their structure and chemical composition, as observed in heart fibers by Browicz (1893), Przewoski (1893), MacCallum (1897), Hoche (1897), Hoyer (1901) and others. If, however, the step-like formations are formed as M. Heidenhain (1902, 1911) affirms "aus parallel gestellten bacillenähnlichen Stäbchen," and "the simplest discs consist of rows of bacillary modified foci on adjacent fibrils" as recently stated by Jordan and Banks (1917, p. 317), then sections tangential to the discs should show the isolated rods cut transversely. Few authors analyse figures of this type. Jordan and Banks, although giving many such figures (their Figs. 7, 8 and 25), nowhere indicate these rods in cross-section. So far as these authors are concerned the discs are more or less homogeneous.

In our preparations sections tangential or oblique to the junctional lines of the Purkinje fibers and the fibers of the myocardium present identical figures. At first the junctional lines, as stated by Jordan and Banks and by other authors, affect only a part of the depth of the fibers. Moreover, they are represented by a network of anastomosed trabeculæ which are relatively thick and readily stainable in red with safranin or fuchsin (more so than the myofibrils). In the narrow spaces of this network is a clear liquid (id, Figs. 7, 13, 17 and 19). This coarse reticulum shows that the myofibrils, at the level of the intercalated discs, have undergone not only modification in structure and in chemical composition but also a special modification in arrangement. Instead of being united into small columns they are condensed and

packed into a system of ramifying and anastomosing bands which represent a meshwork in the spaces of which there exists a clear fluid. It is possible that this fluid corresponds to sarcoplasm or perhaps to a different substance colored black with silver nitrate and comparable to the intercellular substance found in an epithelium. Although as regards the syncytial nature of the myocardium and the atrio-ventricular bundle this problem is fundamental, we are unable to solve it. If at the level of the intercalated discs there exists no trace of intercellular cement, it is apparent that the entire system of cardiac fibers should be considered as a syncytial mass.

We ought also to draw attention to a second type of intercalated discs which are present to the number of two, three or more throughout the length of an elongated Purkinje cell between the two extremities of the cytoplasmic body and even at the level of the nuclear zone. These are accessory intracytoplasmic discs often disposed in terraced arrangement at different levels. They bear no relation to the cell limits and correspond to contraction zones. Many authors interpret in this way all the ladder formations found in the length of cardiac fibers. Among these are v. Ebner (1902), Hoffmann (1909), Arnold (1909), Aimé (1911), Jordan and Steele (1912). In their conclusions Jordan and Banks make the following statement (p. 327): "The new data disclosed in this investigation, namely, the origin of the intercalated discs in relation to surfaces of fusion of previously distinct myocardial elements, need not be prejudiced by a forced association with the hypothesis that the discs are essentially irreversible contraction bands."

Finally, we must remark that sometimes there can be seen an intercalated disc (id, Fig. 19) which subdivides transversely into two, one daughter-cell incompletely separated from its twin (pm). If the disc corresponds to a real intercellular delimitation, figures of this type would prove that a mother-cell can undergo not only a longitudinal cleavage into two daughter-cells, but also that these in their turn can undergo a transverse segmentation into two shorter and probably uninuclear elements.

5. Stages of Transition Between Purkinje Cells and Cardiac Cells (Transitional Cells)

The majority of authors state that the subendocardial plexus of Purkinje fibers may extend into the myocardium, at the same time changing its histological characters. Its branches become gradually thin and finally are reduced to a fiber consisting of a single chain of

cells which elongate and of which the myofibrils increase in number while at the same time the sarcoplasm diminishes in quantity. These transitional cells are followed by true cardiac elements. The transition may occur gradually, although sometimes it takes place abruptly. At other times Purkinje cells may reappear and be intercalated in a transitional zone or even in the first segment of the myocardial fiber. Many authors describe transitional cells of this type: v. Hessling (1854), Koelliker (1854), Aeby (1863), Romiti, Duval (1897), Minervi (1899), Hoyer (1901), Marceau (1902), Hofmann (1902), Tawara, Mönckeberg and the majority of more recent authors.

These transitional cells are represented in Fig. 42. There one can see a Purkinje cell of adult type containing one nucleus at each of its poles (np^{I}, np^{II}) and other elements which have undergone structural changes more and more marked from the right to the left. The myofibrils increase in number, the sarcoplasm becomes less abundant and the transverse striation more marked (pc). The cells become more deeply stained and much resemble the cardiac elements in Fig. 7, but their longitudinal striation remains as pronounced as the transverse. They are transitional stages such as are equally visible (pc) in Figs. 10 and 11, and prove that in the normal human adult Purkinje fibers can develop in such a manner as to become transformed into cardiac cells (cf, Fig. 13). This conclusion is based upon the following three other facts:

1. The great number of myocardial fibers which are found scattered among the Purkinje fibers and recognizable even at a low magnification (cc, Fig. 40). For the most part these elements undoubtedly owe their origin to a transformation of Purkinje cells.

2. The great number of cardiac cells produced, especially in the pathological heart, from the longitudinal asymmetrical cleavage of a mother-cell into two or three daughter elements (asp^{III}, Figs. 22, 23 and 29; $asp^{II}a$, $asp^{III}a$, Fig. 32). Many of these daughter-cells just parting from their twin or already completely separated therefrom show in transverse sections a deeply stained appearance characteristic of the cytoplasm of cardiac cells (cf). The myocardial cell (cc) in Fig. 23 has resulted from an axial differentiation in a Purkinje mother-cell (pm).

3. The existence of plexuses or very complicated muscular meshworks the majority of the trabeculæ of which are formed by cardiac fibers (cf, Fig. 41), by a few occasional Purkinje cells (p) and by

transitional elements (pc). The majority of the cardiac fibers should be considered as originating from the Purkinje fibers.

The origination of transitional cells and their transformation into cardiac elements prove that the Purkinje cell, although of a special structure related to the particular functions which it fulfills, can acquire in the course of its evolution a morphology identical with that of the myocardial elements. Its sarcoplasm always remains capable of becoming differentiated and producing new myofibrils. When the contractility of the heart demands new cardiac fibers, these are furnished by the Purkinje cells which until then functionate in the transmission of the wave of contraction and are constructed accordingly. When the anatomical basis necessary for this transmission is definitely established to the point at which conduction is certain, some Purkinje elements seem to become useless and are capable of being transformed into constituent myocardial parts.

We are in accord with Marceau when he states: "Bien que provenant d'éléments identiques, les cellules cardiaques embryonnaires, ces deux formations (cellules de Purkinje et cellules cardiaques) se différencient l'une de l'autre de très bonne heure et dès lors se développent parallèlement en se rapprochant chacune progressivement d'un type défini" (p. 60). But we must add that in the normal man of 36 years certain Purkinje cells, which have become useless from the point of view of the functions which they should fulfill, develop further and become transformed into cardiac elements. In the pathological heart of a man of 42 years a much greater number of Purkinje cells are undergoing a similar transformation to such a point that it appears to us really pathological. Part of the cardiac trouble in heart-block may be set down to a pathological evolution of these constituent parts of the atrioventricular bundle. One may inquire if alterations of this type do not constitute the principal factor causing more or less transient interferences with cardiac rhythm in persons apparently normal.

6. The Sarcolemma of the Purkinje Cells

We have already stated that Schockaert described around all the Purkinje fibers of the sheep's heart a membrane stained blue with iron hæmatoxylin. It separates the elements one from the other and also from the neighboring connective tissue. Jordan and Banks describe and figure around the cells of the "moderator band" of the beef a sarcolemma generally festooned and state that "the telephragmata are

in intimate union with both the sarcolemma and serrations of the nuclear membrane" (p. 302). Speaking of the "atrio-ventricular connective bundle" they find that "the serrations in the enveloping sarcolemma are fixation artefacts" (p. 304). Round the Purkinje cells in process of fusion to form a Purkinje fiber, Jordan and Banks describe various short discs all along the surfaces of fusion and state that "the connecting membrane represents the fused sarcolemmata of the adjacent fibers" [cells] (p. 308).

We have previously seen that the lateral delimitation of the Purkinje cells of embryonic type and of those of adult type also is brought about by an endomysial membrane of connective-tissue-like structure stained blue by Mallory's method and green with light-green. The transitional cells are separated laterally by a similar membrane (sa, Fig. 42). At all these stages in the evolution of the Purkinje cell there can be found in obliquely longitudinal sections simple endomysial septa connected to the discs Z of neighboring myofibrils in such a manner as to give the appearance of a kind of festooned membrane (sa, Fig. 42). Fig. 9 (enm) shows a similar arrangement in the cells of embryonic type and Fig. 16 (enm to the left) in cells of adult type. If transverse sections of the atrio-ventricular bundle of the normal heart (Figs. 21 and 22) be attentively examined, there is clearly seen in several places a deeply staining membrane surrounding the Purkinje cell and often distinct from the neighboring interstitial connective tissue. It is continuous with the cleavage septum between the daughter-cells (pt^{II}, Fig. 22). In the pathological heart this membrane is even more distinct (asp^{III} and asp^{II}, Fig. 23). It may attain a considerable degree of thickness and constitute a thick sheath continuous between the two daughter-cells (p^{II}, Fig. 24; pc, Fig. 23). Such formations undoubtedly present the greatest similarity to the sarcolemmata described by various authors around the cardiac cells. Reference may be made in this connection to the following authors: Cajal (1888), Oestrich (1894), Hoche (1897), v. Ebner (1902), Heidenhain (1901, 1911), Renaut and Mollard (1905), Irene von Palczewska (1910) and Marie Werner (1910). This membrane is visible in our Fig. 7 (enm) surrounding the cardiac fibers. We shall not discuss at all the connective or cytoplasmic origin of this sarcolemma festooned around the myocardial cells. We shall content ourselves with stating that the Purkinje cells possess no trace of a true cellular membrane formed by their cytoplasm, but that they are circumscribed laterally by a membrane-like connective

system of endomysium which often figures as a false festooned sarcolemma. The marked hypertrophy of these membranes and their consequent sclerosis round many Purkinje cells in the pathological heart (pc, Fig. 23) constitutes another indubitable proof of their connective-tissue nature.

7. Arrangement of the Purkinje Fibers in the Atrio-Ventricular Bundle

This arrangement should be studied in longitudinal sections parallel with the axis of the bundle and in transverse sections of the bundle.

A. longitudinal sections

In longitudinal sections it is readily seen that the Purkinje cells of both atrial and ventricular segments are arranged end to end to produce fibers. These are more or less parallel with each other and with the axis of the bundle. They are bound together by short obliquely placed branches so that in reality they form a network, the parallel limbs of which are much longer than the oblique anastomotic ones. These fibers are only one cell thick and the cell in the normal heart is of greater diameter than a cardiac element. The longitudinal branches of this network may attain the length of myocardial fibers. The spaces of the network are very narrow (Figs. 17, 19, 20, 31 and 42) and occupied by a very small quantity of vascular connective-tissue (endomysium). The spaces are much larger in the myocardium (Fig. 7), but in the pathological heart the interstitial tissue may be hypertrophied and bring about considerable increase in the size of the Purkinje network spaces.

This arrangement of fibers as parallel bands comparable to that of the cardiac fibers does not exist throughout. In various places Purkinje cells tend to group themselves in a particular manner.

1. The short cells of embryonic type arrange themselves end to end to form thick Purkinje fibers resulting in an irregular network with very short trabeculæ and very narrow meshes occupied by an endomysium delimiting the lateral surfaces of the cells (Figs. 1 and 2). Often these cells possess intercrossing (Figs. 3, 4 and 8) or plexiform myofibrils (Figs. 11 and 13).

2. Similar networks may present a more complicated arrangement in that the short cells are distributed radially around a central node.

Such are the cellular plexuses of Purkinje (Fig. 12) or the stellate plexiform formations (Fig. 14).

3. The intercalated or association-cells, generally short and thick, bind the longitudinal muscular bundles to the axis of which these cells are placed obliquely or at right angles. The intercalated cells may assume an arrangement in which the individual elements are more or less parallel with each other (Fig. 10) or bound together in network formation (Figs. 11 and 13).

4. At the right atrio-ventricular junction (Piece 5) in the normal heart and also in that of the pathological organ we have noted a whorl-like arrangement of the fibers. In a section parallel with the bundle at this level many groups of Purkinje fibers can be seen (Fig. 40) of which six are well defined (gr^{i-vi}). The razor has cut the majority of these groups more or less longitudinally, but the bundles or the groups of fibers are oriented each in a different direction to form a whorl. We have noted a spiral arrangement less marked in the left ventricular branch (Piece 8) of the normal heart and in the right ventricular branch (Piece 3) of the pathological organ.

B. TRANSVERSE SECTIONS

In transverse sections one notes immediately at certain levels in the atrio-ventricular bundle that the Purkinje fibers are grouped into fascicles of varying thickness. These are separated by relatively thick connective-tissue septa of the perimysium (pem, Fig. 26) which penetrate into the interior of the bundle where they become continuous with the thinner endomysial septa (enm).

This arrangement in bundles is even better marked in other segments of the normal atrio-ventricular bundle. It is visible in the ventricular segments (Figs. 21, 49 and 50), at the right atrio-ventricular junction (Piece 5; Fig. 40), in the septal wall of the right atrium (Piece 7; Figs. 22 and 43) and in other atrial segments (Figs. 47 and 48). But it may become more accentuated in different parts of the pathological heart because of the hypertrophy of the interfascicular connective-tissue. Our studies show this to be the case in the ventricular segments (Figs. 23, 27, 29 and 45, and especially in Figs. 28, 30, 32, 34 and 46), at the right atrio-ventricular junction (Piece 5; Fig. 44) and in the atrium (Fig. 51).

At certain places where the atrophy of the Purkinje fibers is very pronounced the endomysium may become so thick that the fascicular

arrangement is more or less effaced (Figs. 28, 29 and 32). But in this case there are still generally recognizable groups of two, three or four daughter-cells produced by the longitudinal cleavage of one or two mother-cells. The hypertrophied interfascicular and intrafascicular connective-tissue is sometimes dense and compact, being sclerosed throughout its entire extent (Figs. 28 and 30). In other cases it has more of an areolar appearance and is vascular (Figs. 23 and 29) in which case the pericellular sheath is formed by a denser sclerosed tissue (Figs. 23 and 29).

The fascicular arrangement of the Purkinje fibers is not constant. Quite often there are to be seen areas of normal and pathological atrio-ventricular bundles in which the interfascicular tissue is scarcely thicker than the intrafascicular tissue and in such cases the fibers appear to be more or less equidistant from each other.

The majority of authors agree regarding the existence of a connective-tissue sheath with numerous elastic fibers surrounding several segments of the atrio-ventricular bundle. Among others may be cited v. Hessling (1854), Reichert (1854), Ranvier (1876), Durand (1879), Renaut (1893), Marceau (1902), Tawara (1906), Fahr (1907), De Witt (1909), Lhamon (1912) and King (1916). While some, like Ranvier, Durand and Renaut, claim that the connective-tissue never penetrates between the constituent cells of a trabecula of Purkinje, others insist that it is prolonged between these elements. In the terminal arborizations of the atrio-ventricular bundle of the sheep, Tawara describes, round each strand many cells thick, a fine connective-tissue sheath " die wohl hier und da Septen in das Bündel hineinsendet und förmliche Einkerbungen und Einschnürungen der Oberfläche bedingt, aber nirgends das ganze Bündel in einzelne Fasern zerlegt " (p. 127). According to Fahr the atrio-ventricular bundle in the human embryo contains a more abundant connective tissue than the cardiac muscle. Because of this it is possible to distinguish it from the myocardium. Mall (1912) recognized it in two embryos of 50 mm. length by the appearance of its cells which " are more epithelial " and states that in one of the two " this differentiated band can be followed into both of its divisions, one of which reaches to the moderator band." Further on this author adds, " It is thus seen that the atrio-ventricular bundle is present in an embryo 8 mm. long and that as soon as the muscle of the rest of the atrial canal is broken down it becomes outlined by encircling spaces which are now formed."

In describing the structure in man of the inferior part of the left ventricular branch in which Purkinje fibers exist, Mönckeberg claims that each fiber is surrounded by a delicate connective-tissue sheath which "stellenweise eigenartige septenförmige Fortsätze in die Fasern selbst hineinsendet." But this author in no way recognizes the importance or the significance of these prolongations.

B. ENDOCARDIUM[1]

1. THICKNESS

It is known that the endocardium is much thicker in the atria than in the ventricles. According to v. Ebner (quoted by Schäfer, p. 323) its transverse diameter in the right atrium is five times greater than in the left ventricle. We intend to draw attention to the thickness and to certain details of structure of this endocardium over different segments of the atrio-ventricular bundle. Its transverse diameter varies very greatly according to the area and to the pathological alterations undergone. Three types of endocardium may be distinguished, the first thin, the second of medium thickness and the third thick, but it is evident that all intermediate stages will be encountered.

In the normal heart a thin endocardium is illustrated in Fig. 26 (Piece 10) which represents a transverse section of the base of the left posterior papillary muscle. The endocardium is of a similar type in the moderator band of the right ventricle (Piece 1), at the base of the anterior papillary muscle itself (Piece 2), in the course of the right branch (Piece 3), over the stem (Piece 4) and close to the right atrio-ventricular junction (Piece 5). In the left ventricle the endocardium is thin near the base of the posterior papillary muscle (Piece 10) and at the level of the left posterior branch (Piece 9).

Figs. 49 and 50 (Piece 8) show an endocardium of medium thickness and represent transverse sections of the left posterior ventricular branch near its commencement. The endocardium is of almost the same diameter at the base of the left posterior papillary muscle (Piece 11) and in the neighborhood of the superior vena cava (Piece 15; en, Fig. 48).

The endocardium attains its greatest thickness in the right atrium on the septal wall (Piece 7; en, Fig. 43), in the neighborhood of the coronary opening (Piece 6) and at the right of the atrio-ventricular junction (Piece 5).

[1] See table in Summary, page 53.

From these observations it follows that in the heart of a normal man of 36 years the endocardium is thinner in the right ventricle than in the left, that in general it is very thin in both ventricles, although it may attain a medium thickness at the level of certain portions of the atrio-ventricular bundle in the left ventricle. In the right atrium it is much thicker than in either ventricle, but is only of medium thickness close to the orifice of the superior vena cava.

In the pathological heart the endocardium is markedly thickened in several regions but one must remark that the endocardium may show different appearances in the same section. As an example we may mention the endocardium which covers the stem of the bundle (Piece 4). This portion of the atrio-ventricular bundle is surrounded by a thick layer of dense connective tissue which is in direct continuity with the endocardium (Fig. 46) which consists of a superficial zone of a loose areolar tissue (en) and a thick subjacent zone (ens) of sclerosed tissue. It completely surrounds the bundle and separates it from the neighboring myocardium (lc). Not only does the endocardium attain an extreme thickness in this location but the bundle seems actually to lie within it. Now at a certain distance from the pars membranacea and on each side of the bundle there is to be observed a thin lamina of Purkinje fibers much greater in diameter than those of the bundle itself. This lamina is covered by thin endocardium directly continuous with the less dense of the two layers of endocardium already described in the foregoing part of this paragraph (en, Fig. 46). This structural feature proves that quite often in consequence of hypertrophy or of localized sclerosis the endocardium may increase markedly in thickness in certain sites whereas somewhat lateral to the sclerosed area it becomes suddenly or gradually thinner.

In the pathological heart a thin endocardium occurs in the right ventricle at the surface of the anterior papillary muscle (Piece 2) and in certain locations over the main stem (Piece 4), in the right atrium in certain areas of the septal wall (Piece 7) and close to the orifice of the superior vena cava (Piece 15).

Endocardium of medium thickness in the pathological heart occurs in the right ventricle in the moderator band (Piece 1) and at the surface of the proximal part of the right branch (Piece 3); in the left ventricle over the proximal part of the left posterior branch (Piece 8; en, Fig. 35), over its distal portion (Piece 9; en, Fig. 27) and at the base of the posterior papillary muscle (Piece 10); in the right atrium

upon the septal wall (Piece 7) and certain areas adjoining the orifice of the coronary sinus (Piece 6).

The endocardium attains its greatest thickness in the pathological heart in the atrium on the septum between the coronary orifice and the fossa ovalis (Piece 14; en, Fig. 51; Piece 6) and near the orifice of the superior vena cava (Piece 16). Similarly, it is very thick at the base of the posterior papillary muscle of the left ventricle and over the main stem at the origin of the right ventricular branch (Piece 4; en, Fig. 46).

From the foregoing we note the following facts:

1. In general the endocardium is thinner in the right ventricle than in the left, but it is much thicker in both ventricles of the pathological heart than in those of the normal organ. It therefore participates in the chronic inflammatory process provoked by syphilis.

2. In general the endocardium is thicker in the right atrium than in the ventricles. The difference is not so obvious as in the normal heart, however, because it has not undergone marked hypertrophy or sclerosis as in the case of the ventricles.

We do not intend to make a study of the structure of the endocardium in the human heart. This has been done by several authors. We shall simply refer to the description given by Gustave Mann in Schäfer's Textbook of Histology, 1912, Vol. 2, p. 321, and for the description of layers of smooth muscular fibers and elastic fibers to the works of Nagayo (1909) and of Alexander Gibson (1909).

2. ELASTIC FIBERS

Elastic fibers are very abundant in the endocardium and in certain locations they form two or three networks which tend to result in fenestrated membranes the fibers of which are of very variable diameter. Fig. 52 is from a section obliquely tangential to the surface of the endocardium of the septal wall of the right atrium (Piece 7) in the normal heart. In it may be observed the following features:

1. The superficial endothelial membrane with visible nuclei (nen).

2. Under this there is a thin pale zone, the subendothelial layer formed by bundles of very fine collagenous fibrils.

3. A first elastic membrane (em^{I}) of very delicate fibers ramifying and anastomosing to form a network with narrow meshes resulting in a real fenestrated membrane in certain areas.

4. A second elastic membrane of fibers of medium thickness (em^{II}) underlying the preceding. The spaces of this reticulum are larger,

although in certain areas they become narrowed and the network acquires the characters of a fenestrated membrane.

5. A third elastic network, the deepest of all, of very thick fibers (em^{III}) and large interstices. In some places the meshes become reduced owing to an increase in diameter of the fibers and especially to an enlargement of the nodes of the reticulum. In this layer there likewise appear areas resembling a fenestrated membrane with meshes of variable size.

The first elastic membrane is most clearly seen in Fig. 53 (em^{I}) in the endocardium of medium thickness covering the left posterior branch (Piece 9) of the atrio-ventricular bundle in the pathological heart. The fenestrated membrane appearance in it is very distinct. Fig. 54, a photograph of the same segment (Piece 9 of the pathological heart) shows more clearly the fibrous expansions at the level of the nodes and the appearance of what seems to be a fenestrated membrane close beside other areas with very large interstices.

The three elastic membranes in Fig. 52 are separated by narrow intervals in which the elastic fibers are less numerous and the collagenous fibrillar bundles more abundant. In these two photographs of the pathological heart are visible near the connective-tissue cells (nc, Fig. 54) certain white globules, leucocytes (le, Figs. 53 and 54) and even white globules with polymorph nuclei (lpo, Fig. 53).

It is clear that one cannot find the three elastic membranes in all the different segments of the endocardium especially in the thin areas, but even in these there is a very considerable quantity of elastic filaments. The three figures just mentioned show also that the increase in thickness of the endocardium in the pathological heart is not due solely to the slow formation of a collagenous tissue, but equally to the production of new elastic elements. In certain areas of the hypertrophied endocardium these are as numerous as in the normal tissue.

3. SMOOTH MUSCULAR FIBERS

The inflammatory process appears to have a more detrimental influence upon the smooth muscular fibers. First we must remark that the brief statements made in the tabular summary present only a relative value. In speaking of the existence of a more or less continuous layer of smooth fibers or of two layers in an atrio-ventricular segment we have intended to imply that in certain places or throughout a considerable extent of the segment our preparations show the specified

details of structure. It is to be understood that the smooth fibers never form a tunica media so thick or so continuous as they do in the large arteries.

Reviewing the tabular summary and comparing the different statements there made we are led to the following conclusions:

NORMAL HEART

1. Smooth muscular fibers exist throughout almost the whole extent of the endocardium which covers the various ventricular segments of the atrio-ventricular bundle except the portion related to the right ventricular branch as it lies on the septal wall (Piece 3). Most frequently they occur as isolated scattered fibers near the middle of the thickness of the endocardium, sometimes (Pieces 2 and 8) as cells bound into bundles (scb, Fig. 50) or as bundles united into a more or less continuous layer (Pieces 4 and 8) as in Fig. 49 (lsc). They are a little more numerous in the left ventricle than in the right.

2. The smooth muscle fibers are undoubtedly much more numerous in the right atrium than in the ventricles. Relatively infrequent on the septal wall proper (Piece 7) they form a more or less continuous layer (Piece 6) and even two distinct continuous layers (lsc, Fig. 48) where the atrial branches border upon the orifice of the coronary sinus and of the superior vena cava (Piece 15).

PATHOLOGICAL HEART

1. No smooth muscular fibers are visible at all in the right ventricle or along the stem of the bundle. In the left ventricle they are lacking over the left posterior branch (Piece 9); but there do exist scattered bundles in the three other blocks of tissue from this ventricle (Pieces 8, 10 and 11). In the right atrium there are some isolated fibers or bundles near the opening of the coronary sinus (Pieces 6 and 14) and of the superior vena cava (Piece 15). They are not present upon the septal wall (Piece 7).

2. Smooth muscle fibers are, then, more numerous in the left ventricle than in the right, precisely as we found in the normal heart, but they are undoubtedly much more numerous in the ventricles of the latter than in those of the pathological organ.

3. In the syphilitic heart the smooth muscle fibers are scarcely more numerous in the right atrium than in the left ventricle.

4. As a result of the pathological process the smooth muscle fibers are much rarer in the syphilitic heart than in the normal specimen. We do not know at what age smooth muscle fibers appear in the endocardium and we do not know the precise date at which the patient contracted the syphilis which arrested the development of smooth muscle. We are therefore unable to discuss the question whether or no this tissue had attained its complete development in the syphilitic patient. It appears to us indisputable, however, that the sclerotic process has exercised a marked influence towards atrophy and disappearance of the smooth muscle cells of the endocardium.

In this connection it is interesting to note the sclerosis and atrophy of the tunica media both of the larger arteries and of the smaller arterial branches in the atrio-ventricular bundle. The coronary artery and the two other arterial branches visible in Fig. 44 (as), from Piece 5, possess walls from which the media has completely disappeared, since it has been transformed into a dense connective tissue. In the whole series of sections one cannot find a single normal smooth muscle fiber. In the same figure one sees, however, other small arterial branches which are normal (ar, arc). In the wall of the large artery which runs in the atrio-ventricular bundle (Piece 4) one encounters here and there a normal smooth muscle fiber, but the greatest part of the media is sclerosed (as, Fig. 46), whereas other much smaller branches are unaltered (ar). In the thick bundle of Purkinje fibers from the left posterior papillary muscle (Fig. 45 from Piece 11), a short distance from the vein (v) there is to be seen a completely sclerosed arterial branch (as). Arteries of a considerable size, the seat of a more or less advanced sclerosis of the smooth muscle fibers, are present in the majority of the atrial and ventricular segments of the atrio-ventricular bundle. These lesions must entail profound alterations in the muscular cells to which they carry blood.

We are then forced to the conclusion that the syphilitic process has exercised a detrimental influence upon the muscular fibers of many arteries of the atrio-ventricular bundle and upon those of the neighboring endocardium.

Smooth muscular fibers are rarely met with under the endocardium in the normal heart and even under the layer of Purkinje fibers. In Fig. 50 (Piece 8) may be observed between the thin layers of Purkinje fibers (lp) and the myocardium (lc) two bundles of smooth muscle fibers cut transversely (scb), the one large and the other smaller.

At a suitable magnification these elements show all the characters of smooth muscle cells. There is also another group of them situated likewise between the myocardium and the Purkinje layer in the same Piece 8 of the pathological heart.

The course of the smooth muscle fibers in the endocardium is generally more or less parallel with the axis of the atrio-ventricular bundle, for transverse sections of the bundle cut them transversely (lsc, Fig. 49). But in sections tangential to the internal surface of the endocardium isolated smooth muscle fibers show a tendency to form a netwŏrk (sc, Figs. 56, 57 and 58), while the muscular bundles decussate in different directions (scb, Fig. 55) presenting a whorled arrangement recalling that already described in the case of the bundles of Purkinje fibers (Fig. 40).

In the meshwork of isolated smooth muscle fibers one can note triangular elements of exceptional form (sct, Fig. 56). The nucleus itself generally rod-like (sc, Fig. 56) may assume a triangular form (sct, Fig. 56). Figs. 57 and 58 show us two examples of two smooth fibers anastomosed end to end (sca). In Fig. 58 one of the two elements (sc) united by a fine anastomotic branch is not exactly in focus, but from the preparation one can state positively that the segment sca is certainly continuous with the two cells in question. Examples of anastomosed smooth fibers were described for the first time by Flemming in the bladder of Batrachia.

C. TRACES OF INTERSTITIAL INFLAMMATION IN THE PATHOLOGICAL HEART ALONG THE ATRIO-VENTRICULAR BUNDLE AND IN THE SUPERFICIAL ENDOCARDIUM

The tabular summary shows that in many segments of the bundle there exist traces of an infiltration of lymphocytes and leucocytes, but nowhere does it encroach upon the neighboring myocardium. This slight and diffuse inflammation can be seen at a low magnification (cti) in Figs. 41 (Piece 5) and 45 (Piece 11) and at a greater magnification (cti) in Fig. 24 (Piece 10) and (le) Fig. 12 (Piece 1). It is manifested by the invasion of leucocytes into the connective tissue, the epi-, peri- and endo-mysium and even into the neighboring endocardium. But in certain areas, especially in the left ventricle (Pieces 9, 10 and 11), the infiltration, whether diffuse or localized to certain centers is much more accentuated. Fig. 27 (Piece 9) shows this at a low magnification in the endocardium (cti) and in the zone of Purkinje fibers (cti). It is very pronounced in the Purkinje zone of Fig. 36 (cti).

In Fig. 60 which represents a segment of the endocardium (Piece 9) reproduced at 535 diameters there are recognizable lymphocytes (ly) with a small nucleus rich in chromatin, leucoblasts (le) bulkier with a simple nucleus surrounded by a more abundant protoplasm, and polymorphocytes with a lobed nucleus (lpo). Sometimes one sees even red corpuscles extravasated in quite considerable numbers (rc). Among these cells others are found known as "mast-cells," the protoplasm of which is packed with large granules staining with safranin, but one must remark that this last variety is present to as great an extent in the normal heart as in the pathological specimen.

In examining closely series of preparations in which the endomysium and the perimysium of the atrio-ventricular bundle are invaded by a considerable number of leucocytes we have been surprised to observe that the Purkinje cells generally resist this invasion and remain intact. There are, however, some exceptions as exemplified in Fig. 61. The cell p encloses in a large clear sarcoplasmic zone a mass of leucocytes (le) and two others exhibit leucocytes in their cortical myofibrillar zone (le) while the mother-cell (pm) adjoining is entirely free. Fig. 62 shows a second example of leucocytes enclosed in the sarcoplasm of a Purkinje cell where they undergo a kind of disintegration and karyolysis. This figure seems to show that the Purkinje element is endowed with phagocytic properties which permit it to destroy and to digest the invading cells.

The inflammation, although generally slight and particularly little marked in the right atrium, sufficiently explains the chronic hypertrophy undergone by the interstitial tissue and the endocardium in certain ventricular segments.

We shall dwell scarcely at all upon the fatty degeneration of the Purkinje fibers. Preparations fixed with osmic reagents show in the majority of segments of the atrio-ventricular bundle numerous groups of Purkinje fibers, the sarcoplasmic and cortical zones of which are packed with black, fatty granulations soluble in turpentine. But we must also note that the normal heart shows identical alterations induced by the pneumococcic infection. Fatty degeneration does not represent an alteration peculiar to heart-block, and Bullard (1916) has just demonstrated that "neutral fat is of normal occurrence in the muscle fibers of the bundle of His."

D. ENIGMATIC ELEMENTS

Before concluding this work we must draw attention to the occurrence of two enigmatic elements found, one in the pathological heart and the other in the normal organ. The first is represented in Figs. 59 and 65 (pel) representing, respectively, a transverse and a longitudinal section of a cardiac cell close to the Purkinje zone. One encounters these enigmatic elements only in the neighborhood of the orifice of the superior vena cava (Piece 16) and nowhere else. In the middle of the cell body there is seen a cluster or a sort of spireme formed by an interlacement of convoluted and spiral filaments of variable thickness and easily stainable with iron hæmatoxylin. In normal tissues there are but two kinds of elements which resemble even vaguely those of the two figures in question. First there are the chromosomes or chromatic clusters of a nucleus in mitosis. In the present case, however, there can be no question of karyokinesis, for the nucleus is in a resting condition and is visible to one side of the cluster (nca, Fig. 59). Secondly, in ovarian ova in the stage of growth in the bat (Vesperugo noctula, one of us (O. V. d. S., 1905), has described as " pseudochromosomes " certain convoluted and spiral filaments all around the yolk body and presenting an appearance somewhat similar to those of Figs. 59 and 65. These pseudochromosomes are formed in reality by accumulations of mitochondria (O. V. d. S., 1904). In spite of the resemblance of the enigmatic clusters to these pseudochromosomes we cannot consider them as formations of the same nature: indeed they are localized exclusively to a small segment of the myocardium and are in no wise generally distributed. This observation causes us to believe that the cluster represents rather a parasitic element. When one considers the nature of the disease from which the patient was suffering one naturally thinks of treponemata. Professor W. G. MacCallum has kindly examined these preparations but he is unable to recognize treponemata in the cluster. We must therefore content ourselves with stating that this formation is an enigmatic cluster probably of parasitic nature.

A second type of elements found only in the normal heart is visible especially at the level of the left branch just as it enters the ventricle (Piece 8) and of its posterior subdivision (Piece 9) in the substance of the bundle itself. These elements occur in the interior of the Purkinje cells of adult type and are represented by Figs. 63 and 64 (e). They are elongated oval bodies sometimes slightly swollen towards the middle. They are stained deeply with safranin and their

structure is in great part homogeneous like that of the red corpuscles visible in a neighboring capillary (cprc, Fig. 63). They often contain one or more small vacuoles filled with a pale liquid. They occur scattered to the number of from two or three to ten along the axial sarcoplasm of the Purkinje cell. In Fig. 64 one can count eight. Examined at a low magnification they resemble crystalloid bodies described as occurring in the genital glands and other organs which, however, present a more regular form and are represented by finer rods. They may be parasites though we cannot definitely so state. In a few preparations fixed in Flemming's fluid we have succeeded in staining with safranin the axial cytoplasmic band described in the earlier part of this paper as occurring in the Purkinje cells (st, Figs. 5 and 23). This axial strand presents a homogeneous structure which recalls that of the enigmatic elements (e) of Figs. 63 and 64. It may be that this filament can undergo fragmentation into numerous elements comparable with these enigmatic bodies, but we have been unable to discover different stages of any such fragmentation and we therefore doubt its possibility. We must in consequence refrain from any further statement upon the matter.

VI. SUMMARY

1. In the atrio-ventricular bundle in the normal heart of a man of 36 years and in the pathological heart of a man of 42 years we distinguish three varieties of Purkinje cells.

a. Cells of embryonic type, polyhedral or with the long axis somewhat exceeding the diameter. These contain several nuclei which may be clustered together or may show a tendency to deviate along the cell axis and into the lateral parts of the cytoplasm. These nuclei are surrounded by a central or axial sarcoplasmic zone, exceedingly poor in myofibrils, around which there is a cortical layer containing more numerous myofibrils. In regard to the course of these it is possible to distinguish cells with parallel myofibrils, cells with intercrossing myofibrils and cells with plexiform myofibrils which decussate in various directions. The two last mentioned types of elements constitute an anatomical basis which is important from the point of view of transmission of the contraction wave in different directions. Two other formations also present a noteworthy arrangement from this point of view: the intercalated or association cells the axis of which is at right angles or obliquely placed to that of the longitudinal muscular

bundles which they unite, and the cellular plexuses (occasionally stellate in appearance) of Purkinje.

b. Cells of adult type much longer than the foregoing and of which many are particularly bulky. These contain many nuclei which tend to distribute themselves laterally and through the length of the cell body like the nuclei of the embryonic type of cell. From this tendency it results that the element originally with a single axis becomes bipartite or tripartite; it possesses two or three axial bands of sarcoplasm towards each extremity of which are to be observed one or two nuclei. The myofibrillar cortical layer invades the central granular sarcoplasm and produces myofibrillar partitions which separate the two or three sarcoplasmic segments and accentuate in this way the multipartite character of the Purkinje cell.

c. Purkinje cells of transitional type showing stages of transition between Purkinje elements and myocardial cells.

2. Whatever may be the degree of evolution of a Purkinje cell it can always be distinguished from a cardiac cell by the abundance of its sarcoplasm which separates its myofibrils or fibrillar columns. Hence cut longitudinally it presents a longitudinal striation more accentuated than the transverse, whereas in myocardial fibers the transverse striation is predominant, although an isolated myofibril from a Purkinje cell shows transverse striation identical with that of the myofibrils of the myocardium.

3. All the muscular cells of the atrio-ventricular bundle possess the fundamental feature just mentioned. In the atrial segments the myofibrils are generally more regularly distributed throughout the large mass of protoplasm, whereas in the ventricular areas they occupy a cortical zone more or less distinct from the axial sarcoplasmic layer. But cells of the first type are also to be found in the ventricles and representatives of the second type occur in the right atrium. For these reasons it appears to us logical to include all these cells under the heading Purkinje cells.

4. Bulky Purkinje cells are capable of undergoing a longitudinal division or cleavage into smaller daughter-elements by the extension of the neighboring endomysium through the cell body. In this manner a bipartite or tripartite mother-cell divides into two or more smaller elements, multinucleated and more or less symmetrical or else completely asymmetrical in size and structure. In the last mentioned case one of the daughter-cells may present the structure of a transitional element

or indeed of a cardiac element while the other retains the primitive features of the Purkinje cell.

5. Longitudinal cleavage of Purkinje cells is manifested in the normal heart, but in the syphilitic organ it is so marked that it must be considered pathological. Because of the hypertrophy of the interstitial connective-tissue the cleavage affects a much greater number of Purkinje cells and constitutes the most important factor in the atrophy and disappearance of many of these elements.

6. In the pathological heart the connective-tissue septum (endomysium) of cleavage can undergo a considerable thickening and invade the neighboring daughter-cells in its turn, subdividing them into smaller symmetrical or asymmetrical elements the diameter of which hardly surpasses that of a smooth muscle cell. These markedly atrophied cells still possess, when they have retained the features of Purkinje type, a myofibrillar cortical layer and an axial sarcoplasmic zone between which there often appears an internal cytoplasmic membrane.

7. The atrophied elements in their turn may undergo a cleavage into smaller fragments which may be nucleated or on the other hand devoid of nuclei. The latter type represents the last vestiges of the Purkinje cell before its disappearance or complete sclerosis.

8. The pathological cleavage of the Purkinje cell may be accompanied by an amitotic division of the nucleus induced by the extension of the endomysial septum and in certain cases blood capillaries seem to play a predominant rôle in the invasion by the endomysium.

9. The Purkinje cells of adult and of transitional type place themselves end to end to form Purkinje fibers parallel with the axis of the atrio-ventricular bundle and are bound together by short oblique branches. The short cells of embryonic type form a network the fibers or trabeculæ of which are much shorter and the meshes narrower. All these elements are delimited laterally by the interstitial connective tissue which fills the spaces of the network and at their extremities by intercalated discs across which the myofibrils pass continuously from one cell to another. These transverse discs present the same structure and the same significance as those of the cardiac fibers. They do not traverse the entire thickness of the Purkinje cell. They are formed by thick segments of myofibrils and by a special clear substance. When these discs are seen from the surface one can observe that the myofibrils are condensed into a system of thick bands anas-

tomosed to form a network in the spaces of which there exists a clear fluid. We cannot say whether this liquid represents a part of the sarcoplasm or an intercellular substance. The solution of this problem would permit us to determine the syncytial or cellular nature of heart fibers.

10. Purkinje cells present a special morphology in accordance with the special functions which they fulfill. They possess the power of evolving and of transforming themselves into cardiac elements even in the normal state but in the pathological condition this process of transformation may become so accentuated that it appears to us as possibly constituting an important factor in the production of derangements of cardiac rhythm.

11. Surrounding the Purkinje cells laterally there is a very thin endomysial membrane which is continuous with the cleavage partitions appearing in the division of a mother-cell. It often presents a plainly festooned appearance, the discs Z of the neighboring myofibrils being attached along its internal aspect. It should be considered as a production not of the peripheral cytoplasm of the muscular cell but of the neighboring endomysium. It corresponds then to a kind of false sarcolemma. In the pathological condition this sarcolemma may undergo a considerable hypertrophy and with the sclerosed interstitial connective-tissue it forms a second very important factor which in the process of cleavage may exercise a marked influence toward the atrophy of the Purkinje elements.

12. The arrangement of the Purkinje fibers in bundles separated by an interfascicular perimysium thicker than the intrafascicular endomysium is apparent in many areas of different segments of the atrioventricular bundle. At the level of the pars membranacea septi or right atrio-ventricular junction bundles or groups of fibers all more or less parallel with the axis of the main bundle present a special whorled disposition.

13. The endocardium which covers different segments of the atrioventricular bundle presents a variable thickness. In the normal heart it is notably thicker in the right atrium than in the ventricles and it is thicker in the left ventricle than in the right. In the syphilitic heart it has undergone a considerable hypertrophy in the ventricular areas especially in the left ventricle. It therefore participates in the sclerotic process which affects the atrio-ventricular bundle.

14. Elastic fibers are very abundant in this endocardium and in certain locations they produce three successive networks which tend to become transformed into fenestrated elastic membranes. The increase in diameter of the pathological endocardium is due not only to the formation of new collagenous bundles, but also to the production of numerous elastic elements.

15. The endocardium related to the different segments of the atrio-ventricular bundle may include isolated scattered smooth muscular fibers, isolated bundles or sometimes more or less continuous layers of smooth muscle fibers. In the normal heart they are much more numerous in the atrium than in the two ventricles and a little more numerous in the left ventricle than in the right. In the syphilitic heart they are markedly diminished in number in the two ventricles and even in the atrium. There seems to us no doubt that the sclerotic process has exercised a considerable influence toward their reduction in number.

The larger vessels of the arterial circle at the atrio-ventricular junction (Pieces 4 and 5) as well as several small arteries belonging to the atrial and ventricular segments present similar sclerotic lesions; their tunica media is partially or entirely transformed into a fibrous layer.

16. In the pathological heart there exist traces of a slight diffuse inflammation along the majority of the segments of the atrio-ventricular bundle and its superficial endocardium. At certain levels in the left ventricle are to be observed centers of much more marked infiltration.

17. Sclerotic lesions of the interstitial connective-tissue and of the small arterial branches, atrophy of the Purkinje fibers and diffuse inflammation are much more accentuated in the ventricles than in the atrium and particularly in the left ventricle (Pieces 9, 10 and 11).

VII. GENERAL ABBREVIATIONS

ac,	fat cells.
ap,	atrophied Purkinje cells.
ap^{11},	group of two atrophied Purkinje cells.
ar,	artery.
arc,	artery filled with red blood corpuscles.
as,	artery affected by sclerosis.
asp,	asymmetrical Purkinje cells.
asp^{11},	group of two asymmetrical Purkinje cells (daughter-cells).
asp^{111},	group of three asymmetrical Purkinje cells (daughter-cells).

asp^{II}a, two asymmetrical atrophied Purkinje cells (daughter-cells).
asp^{III}a, three asymmetrical atrophied Purkinje cells (daughter-cells)
cc, cardiac cells.
cc^{II}, two daughter-cells of the cardiac type.
cf, cardiac fibers.
con, continuity of myofibrils between two different muscle cells.
cp, capillary.
cpc, capillary filled with red blood corpuscles.
ct, connective tissue.
cti, infiltrated connective tissue.
cts, connective tissue affected by sclerosis.
df, Purkinje cell with intercrossing myofibrils.
e, enigmatic element.
em^{I}, inner elastic fenestrated membrane or elastic network.
em^{II}, middle elastic fenestrated membrane or elastic network.
em^{III}, outer elastic fenestrated membrane or elastic network.
en, endocardium.
enm, endomysium.
ens, endocardium affected by sclerosis.
fg, fat granules.
gr, bundle or group of Purkinje fibers.
gr^{I-VI}, six groups of Purkinje fibers in whorl.
id, intercalated disc.
im, internal cytoplasmic membrane.
lc, layer of cardiac fibers.
le, leucocyte.
lp, layer of Purkinje cells.
lpo, polymorphocyte.
lsc, layer of smooth muscle cells.
ly, lymphocyte.
m, mitochondria.
n, nucleus.
nc, nucleus of connective-tissue cell.
nca, nucleus of cardiac cell.
nen, nucleus of endothelial cell.
np, nucleus of Purkinje cell.
np^{I}, np^{II}, np^{III}, np^{IV}, np^{V}, various nuclei in one Purkinje cell.
npc, nucleus of transitional cell.
p, Purkinje cell.
p^{I}, first daughter Purkinje cell.
p^{II}, second daughter Purkinje cell or group of two daughter Purkinje cells.
p^{III}, group of three daughter Purkinje cells.

pc, cell in transition between Purkinje and cardiac type.
pc^{II}, two daughter-cells of transitional type.
pel, enigmatic cluster.
pem, perimysium.
pig, pigment granules.
pm, Purkinje mother-cell.
pl, Purkinje cell containing a plexus of myofibrils.
pt^{II}, Purkinje mother-cell divided into two parts.
pt^{III}, Purkinje mother-cell divided into three parts.
pt^{IV}, Purkinje mother-cell divided into four parts.
rbr, right branch of the atrio-ventricular bundle.
rc, red blood corpuscle.
sa, sarcolemma.
sc, smooth muscle cell.
sca, anastomosis of two smooth muscle cells.
scb, bundles of smooth muscle cells.
sct, triangular smooth muscle cells.
st, axial cytoplasmic strand in a Purkinje cell.
v, vein.
vrc, vein filled with red blood corpuscles.

VIII. EXPLANATION OF FIGURES[1]

PLATE 1

1. Section tangential to the surface of the endocardium covering the posterior papillary muscle of the left ventricle (Piece 11) of the normal heart. Hermann's fluid, Mallory's stain; magnification 476 diameters.

2. Section tangential to the surface of the endocardium covering the posterior papillary muscle of the left ventricle (Piece 11) of the normal heart. Hermann's fluid, iron hæmatoxylin, Congo red; magnification 476 diameters.

3, 4. Sections tangential to the surface of the endocardium of the right atrio-ventricular junction (Piece 5) in the normal heart. Hermann's fluid, Mallory's stain; magnification 476 diameters.

5, 6. Sections tangential to the surface of the endocardium over the left posterior ventricular branch of the bundle (Piece 9) of the pathological heart. Hermann's fluid, iron hæmatoxylin, Congo red; magnification 476 diameters.

7. Section tangential to the surface of the endocardium covering the posterior papillary muscle of the left ventricle (Piece 11) of the normal heart. Hermann's fluid, Mallory's stain; magnification 476 diameters.

PLATE 2

8. Section tangential to the surface of the endocardium of the moderator band in the right ventricle (Piece 1) of the normal heart. Bouin's fluid, Mallory's stain; magnification 476 diameters.

[1] A reduction of one-eighth has been made in the figures.

9. Section tangential to the surface of the endocardium of the moderator band in the right ventricle (Piece 1) of the normal heart. Hermann's fluid, safranin, light green; magnification 476 diameters.

10, 11. Sections tangential to the surface of the endocardium of the moderator band in the right ventricle (Piece 1) of the normal heart. Bouin's fluid, iron hæmatoxylin, Congo red; magnification 476 diameters.

12, 13. Sections tangential to the surface of the endocardium of the moderator band in the right ventricle (Piece 1) of the normal heart. Bouin's fluid, Mallory's stain; magnification 476 diameters.

PLATE 3

14. Section tangential to the surface of the endocardium of the moderator band in the right ventricle (Piece 1) of the normal heart. Bouin's fluid, iron hæmatoxylin, Congo red; magnification 476 diameters.

15. Section tangential to the surface of the endocardium of the moderator band in the right ventricle (Piece 1) of the normal heart. Bouin's fluid, Mallory's stain; magnification 476 diameters.

16. Section tangential to the endocardium of the right atrio-ventricular junction (Piece 5) of the normal heart. Hermann's fluid, safranin, light green; magnification 476 diameters.

17, 18, 19. Sections tangential to the surface of the endocardium covering the left ventricular branch of the bundle immediately below the aortic cusp (Piece 8) in the normal heart. Flemming's liquid, safranin, light green; magnification 476 diameters.

PLATE 4

20. Section tangential to the surface of the endocardium over the left posterior ventricular branch of the bundle (Piece 9) of the pathological heart. Hermann's fluid, iron hæmatoxylin, Congo red; magnification 476 diameters.

21. Transverse section of the left posterior ventricular branch in the trabecular tissue (Piece 10) in the normal heart. Hermann's fluid, safranin, light green; magnification 535 diameters.

22. Transverse section of the septal wall of the right atrium (Piece 7) of the normal heart. Hermann's fluid, safranin, light green; magnification 476 diameters.

23. Transverse section of the left posterior ventricular branch in the trabecular tissue (Piece 10) of the pathological heart. Hermann s fluid, Mallory's stain; magnification 476 diameters.

PLATE 5

24. Transverse section of the left posterior ventricular branch in the trabecular tissue (Piece 10) of the pathological heart. Hermann's fluid, iron hæmatoxylin, Congo red; magnification 476 diameters.

25. Transverse section through the left posterior ventricular branch of the bundle in the septal wall (Piece 9) of the pathological heart. Hermann's fluid, Mallory's stain; magnification 535 diameters.

26. Transverse section of the left posterior ventricular branch in the trabecular tissue (Piece 10) of the normal heart. Hermann's fluid, safranin, light green; magnification 85 diameters.

27. Transverse section through the left posterior ventricular branch of the bundle in the septal wall (Piece 9) of the pathological heart. Hermann's fluid, safranin, light green; magnification 85 diameters.

PLATE 6

28, 29, 30. Transverse sections through the left posterior ventricular branch of the bundle in the septal wall (Piece 9) of the pathological heart. Hermann's fluid, Mallory's stain; magnification 535 diameters.

31. Section tangential to the surface of the endocardium of the moderator band in the right ventricle (Piece 1) of the normal heart. Bouin's fluid, Mallory's stain; magnification 476 diameters.

32. Transverse section of the stem of the bundle (Piece 4) of the pathological heart. Flemming's liquid, iron hæmatoxylin, Congo red; magnification 476 diameters.

33. Section tangential to the surface of the septal wall of the right atrium (Piece 7) of the pathological heart. Trichloracetic acid, Mallory's stain; magnification 476 diameters.

PLATE 7

34. Transverse section of the stem of the bundle (Piece 4) of the pathological heart. Flemming's liquid, iron hæmatoxylin, Congo red; magnification 476 diameters.

35. Transverse section of the left ventricular branch of the bundle immediately below the aortic cusp (Piece 8) of the pathological heart. Bouin's fluid, Mallory's stain; magnification 103 diameters.

36. Section tangential to the surface of the endocardium covering the left posterior ventricular branch of the bundle in the septal wall (Piece 9) of the pathological heart. Bouin's fluid, Mallory's stain; magnification 103 diameters.

37. Section tangential to the surface of the endocardium covering the left posterior ventricular branch of the bundle in the septal wall (Piece 9) of the pathological heart. Bouin's fluid, Mallory's stain; magnification 476 diameters.

38. Transverse section of the wall of the right atrium including the orifice of the coronary sinus (Piece 6) in the pathological heart. Flemming's liquid, safranin, light green; magnification 476 diameters.

39. Transverse section of the left ventricular branch of the bundle immediately below the aortic cusp (Piece 8) of the normal heart. Flemming's liquid, safranin, light green; magnification 476 diameters.

40. Section tangential to the surface of the endocardium of the right atrio-ventricular junction (Piece 5) of the normal heart. Hermann's fluid, safranin, light green; magnification 103 diameters.

PLATE 8

41. Longitudinal section of the bundle at the pars membranacea septi (Piece 5) of the pathological heart. Hermann's fluid, Mallory's stain; magnification 103 diameters.

42. Section tangential to the surface of the endocardium covering the left posterior ventricular branch in the trabecular tissue (Piece 10) of the normal heart. Hermann's fluid, Mallory's method; magnification 476 diameters.

43. Transverse section of the septal wall of the right atrium (Piece 7) in the normal heart. Hermann's fluid, safranin, light green; magnification 103 diameters.

44. Transverse section of the right atrio-ventricular junction (Piece 5) of the pathological heart. Trichloracetic acid, Mallory's stain; magnification 45 diameters.

PLATE 9

45. Transverse section of the base of the posterior papillary muscle of the left ventricle (Piece 11) in the pathological heart. Bouin's fluid, Mallory's stain; magnification 103 diameters.

46. Transverse section of the stem of the bundle (Piece 4) of the pathological heart. Flemming's liquid, Mallory's stain; magnification 103 diameters.

47. Transverse section of the crista terminalis at the orifice of the superior vena cava (Piece 15) of the normal heart. Flemming's liquid, Mallory's stain; magnification 476 diameters.

48. Transverse section of the crista terminalis at the orifice of the superior vena cava (Piece 15) of the normal heart. Flemming's liquid, Mallory's stain; magnification 103 diameters.

PLATE 10

49, 50. Transverse sections of the left ventricular branch of the bundle immediately below the aortic cusp (Piece 8) of the normal heart. Flemming's liquid, safranin, light green; magnification 103 diameters.

51. Transverse section of the interatrial septum between coronary orifice and fossa ovalis (Piece 14) of the pathological heart. Bouin's fluid, Mallory's stain; magnification 103 diameters.

52. Section tangential to the surface of the endocardium of the septal wall in the right atrium (Piece 7) of the normal heart. Hermann's fluid, iron hæmatoxylin, Congo red; magnification 476 diameters.

53. Section tangential to the surface of the endocardium covering the left posterior ventricular branch of the bundle in the septal wall (Piece 9) of the pathological heart. Hermann's fluid, iron hæmatoxylin, Congo red; magnification 476 diameters.

PLATE 11

54. Section tangential to the surface of the endocardium covering the left posterior ventricular branch of the bundle in the septal wall (Piece 9) of the pathological heart. Hermann's fluid, iron hæmatoxylin, Congo red; magnification 476 diameters.

55. Section tangential to the surface of the endocardium covering the left ventricular branch of the bundle immediately below the aortic cusp (Piece 8) of the normal heart. Flemming's liquid, Mallory's stain; magnification 103 diameters.

56, 57, 58. Sections tangential to the surface of the endocardium covering the right atrio-ventricular junction (Piece 4) of the normal heart. Bouin's fluid, Mallory's stain; magnification 476 diameters.

59. Transverse section of the margin of the superior vena caval orifice (Piece 16) of the pathological heart. Bouin's fluid, iron hæmatoxylin, Congo red; magnification 476 diameters.

PLATE 12

60. Transverse section of the endocardium covering the left posterior ventricular branch of the bundle in the septal wall (Piece 9) of the pathological heart. Hermann's fluid, Mallory's stain; magnification 535 diameters.

61. Transverse section of the left posterior ventricular branch of the bundle in the septal wall (Piece 9) of the pathological heart. Bouin's fluid, iron hæmatoxylin, Congo red; magnification 476 diameters.

62. Transverse section of the left posterior ventricular branch of the bundle in the septal wall (Piece 9) of the pathological heart. Bouin's fluid, Mallory's stain; magnification 476 diameters.

63. Section tangential to the surface of the endocardium covering the left ventricular branch of the bundle immediately below the aortic cusp (Piece 8) of the normal heart. Flemming's liquid, Mallory's stain; magnification 476 diameters.

64. Section tangential to the surface of the endocardium covering the left ventricular branch of the bundle immediately below the aortic cusp (Piece 8) of the normal heart. Flemming's liquid, safranin, light green; magnification 476 diameters.

65. Transverse section of the margin of the superior vena cava orifice (Piece 16) of the pathological heart. Bouin's fluid, iron hæmatoxylin, Congo red; magnification 476 diameters.

PLATE 13

66. Heart 1 opened to show areas from which tissue blocks were removed for histological examination (see p. 4) of right side.

67. Heart 1 opened to show areas from which tissue blocks were removed for histological examination (see p. 5) of left ventricle.

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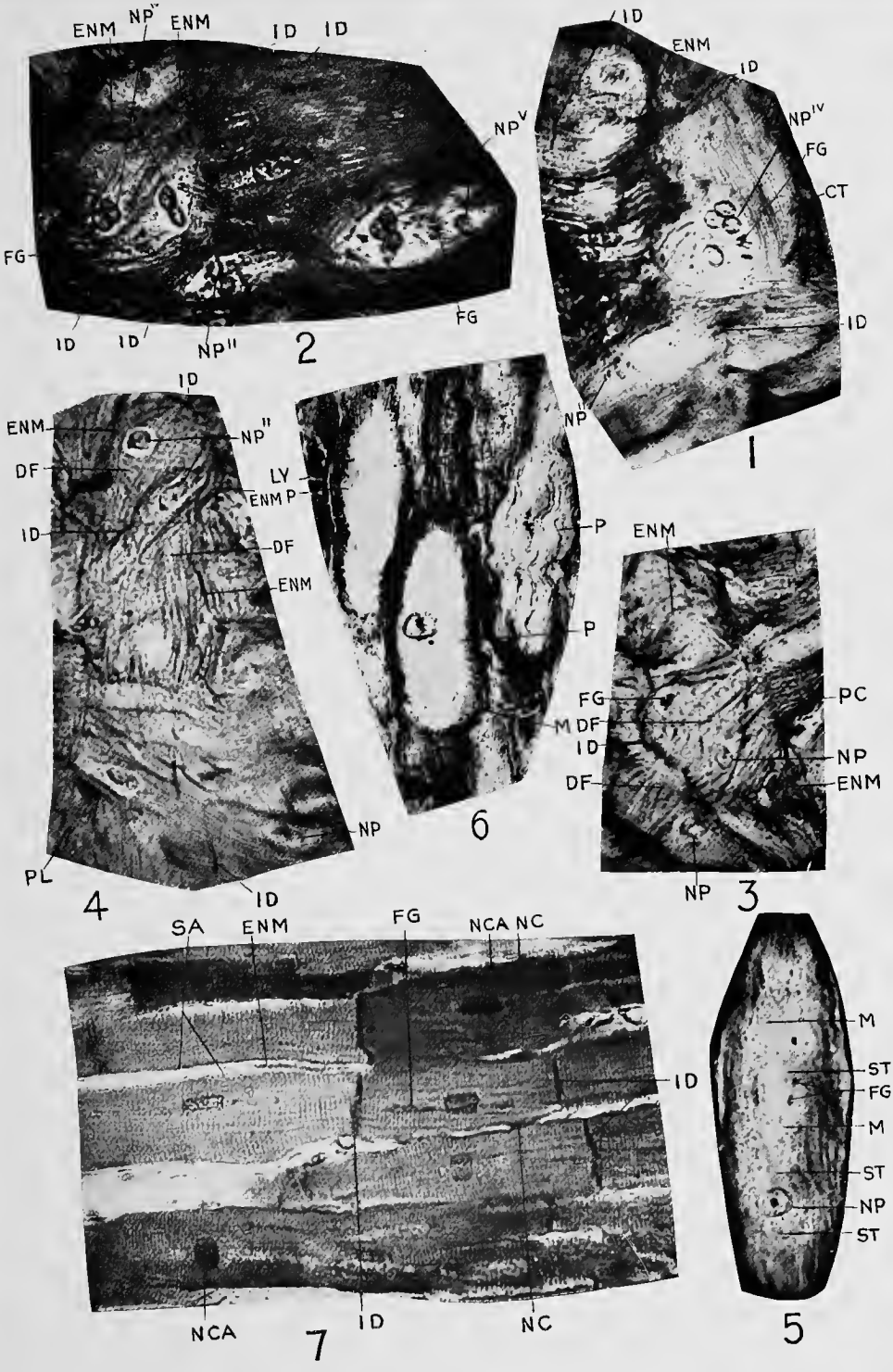
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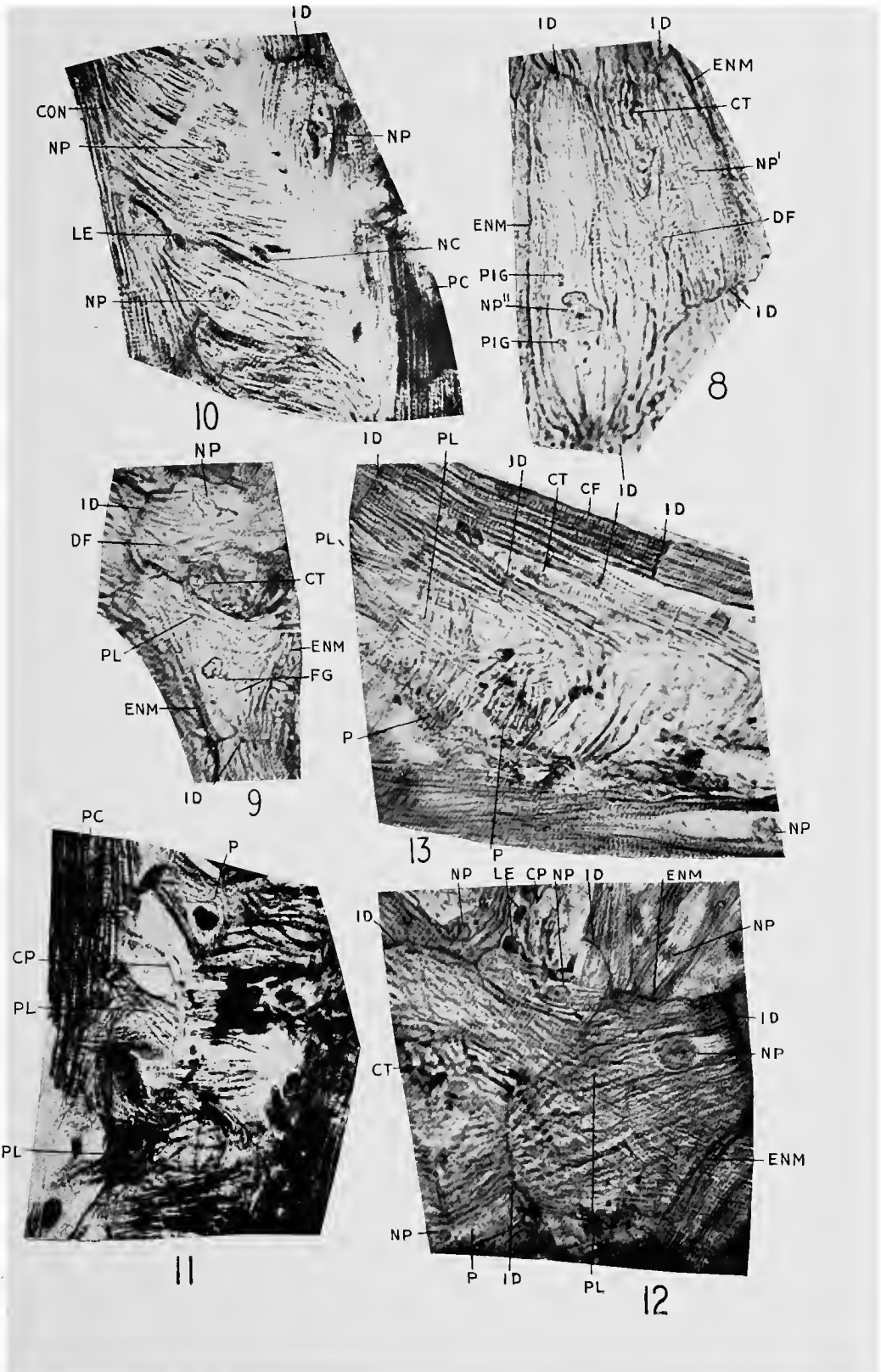
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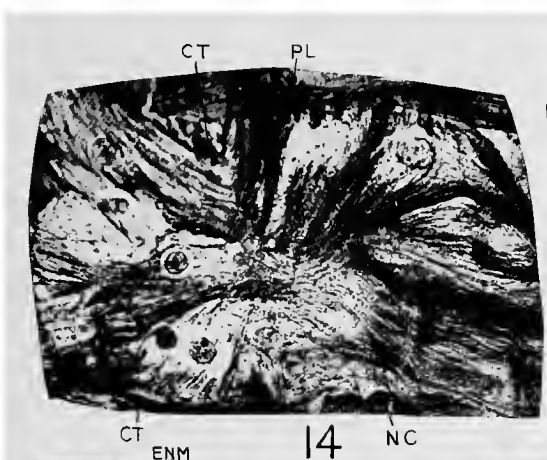

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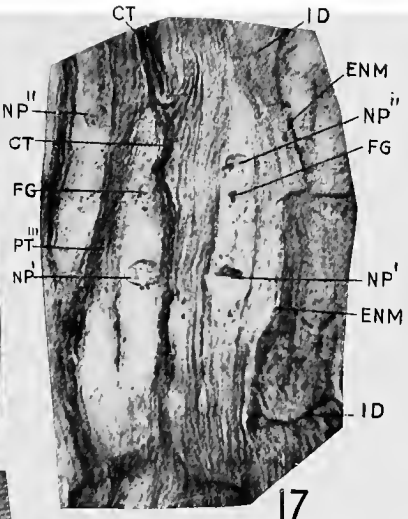

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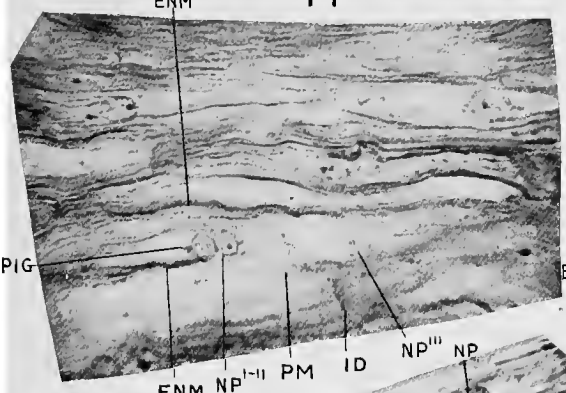

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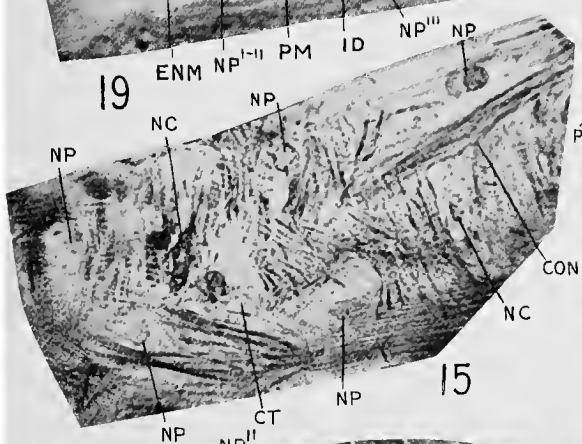

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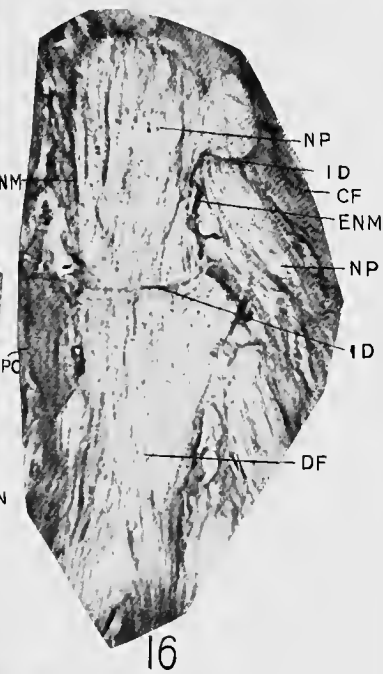

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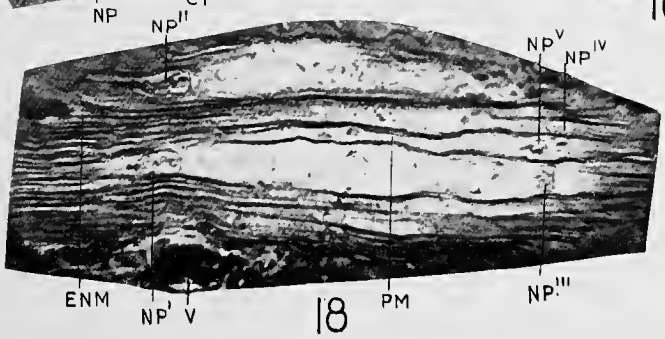

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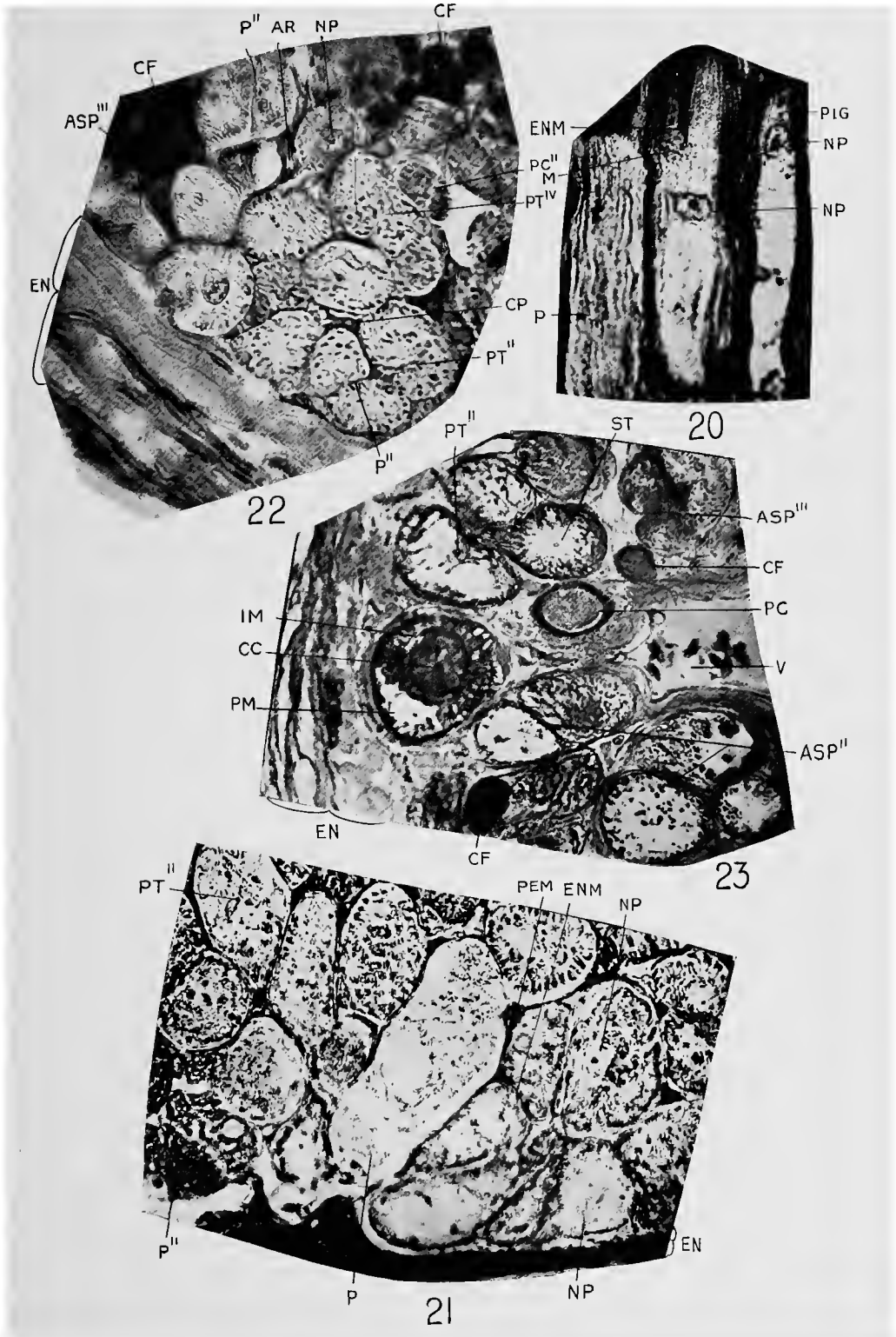
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CP
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P''
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NP
P
20
PT''
ST
ASP'''
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PT''
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ENM
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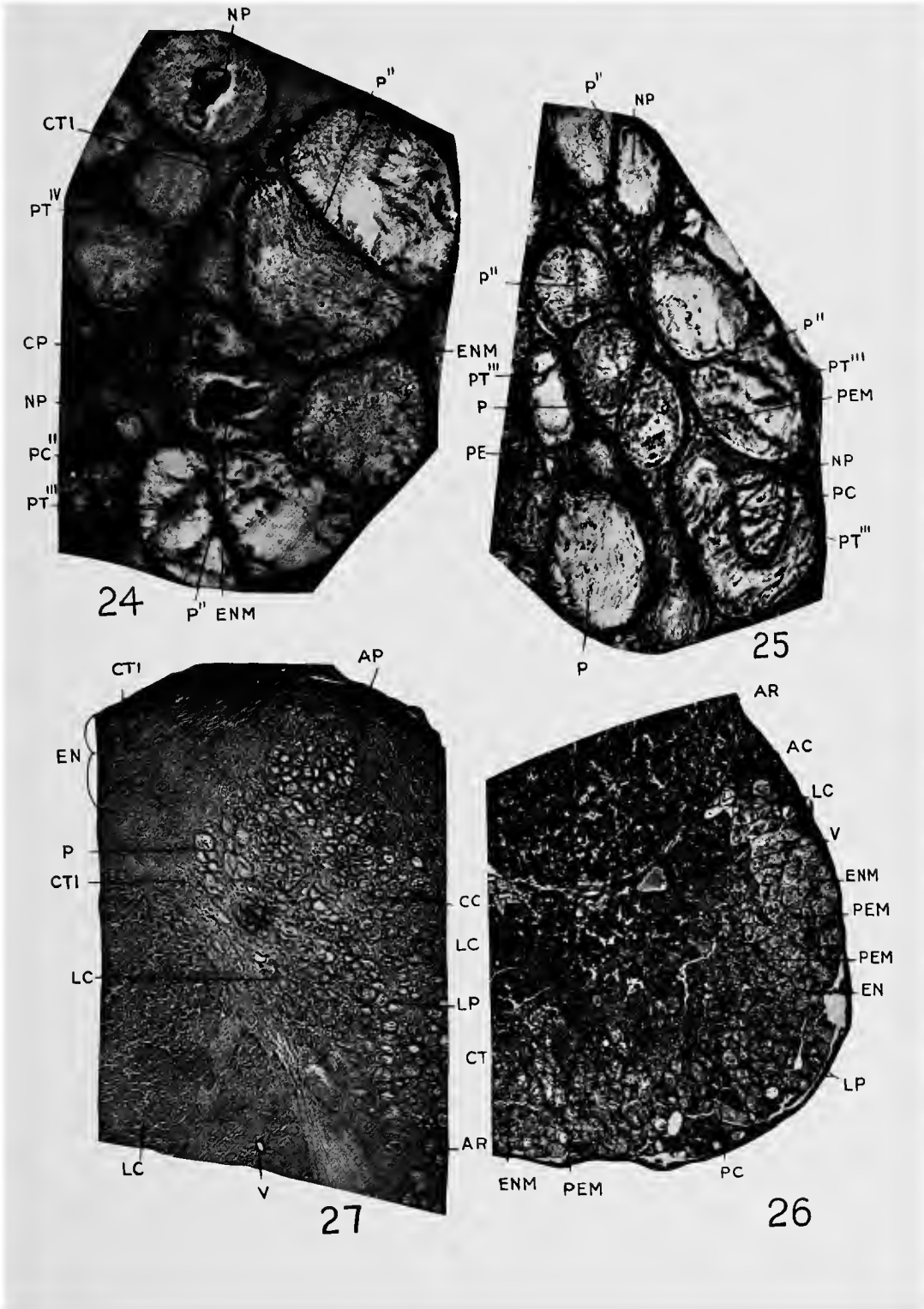
P''
P
NP
EN
21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CP
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PT'''
P'' ENM
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P'
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PEM
PT'''
P
PE
NP
PC
PT'''
P
25
CTI
AP
EN
P
CTI
LC
LC
V
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PC
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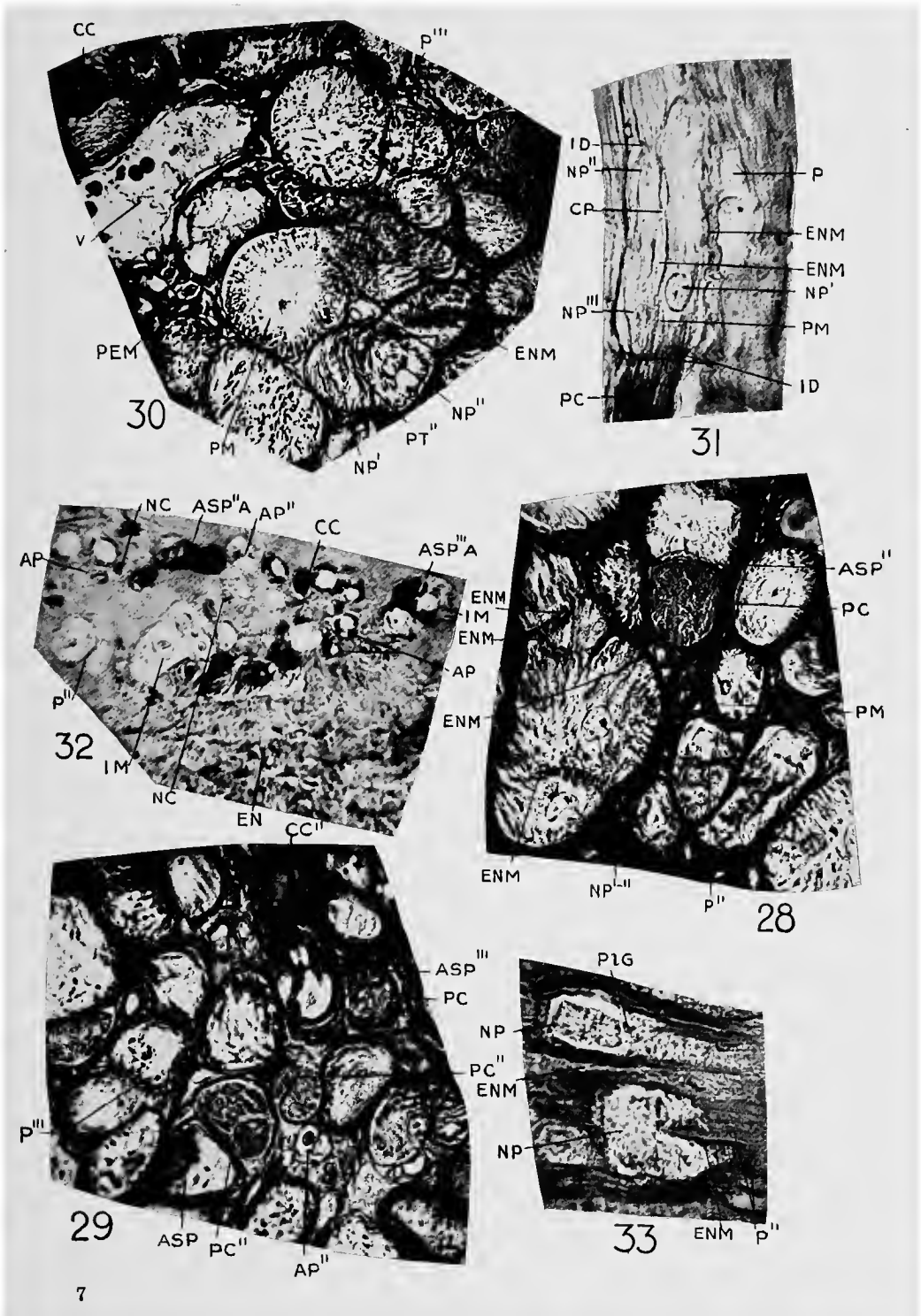
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PT''
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NP'
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ID
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P
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ENM
ENM
NP'
NP'''
PM
ID
PC
31
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ASP''A
AP''
CC
AP
ASP'''A
ENM
IM
ENM
AP
P''
32
IM
NC
EN
CC''
ASP''
PC
PM
ENM
ENM
NP'''
P''
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AP''
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ENM
P''
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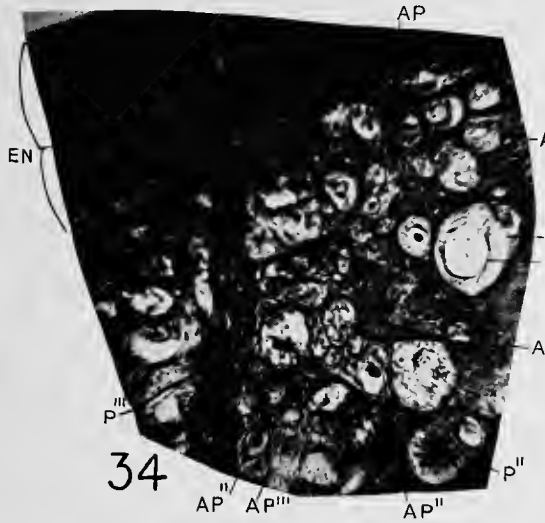

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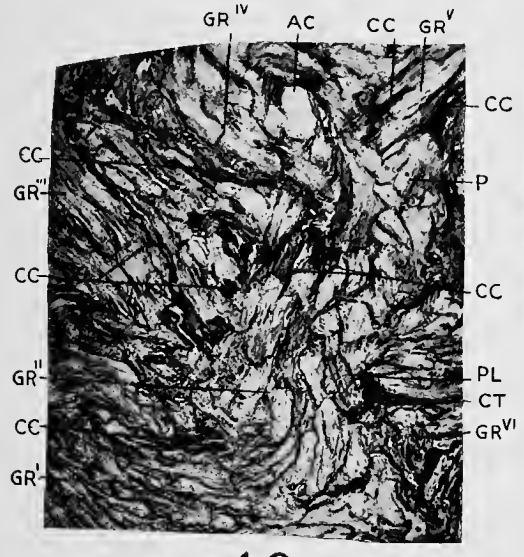

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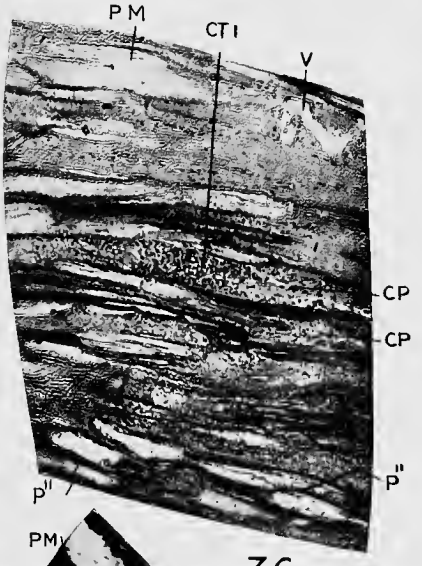

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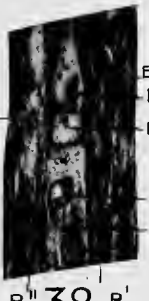

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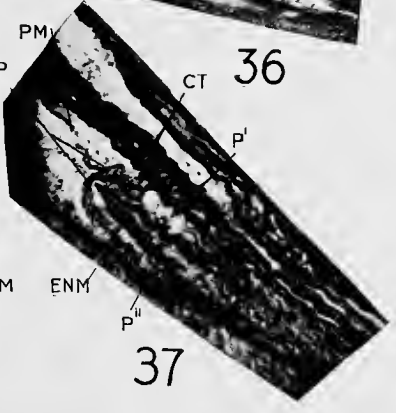

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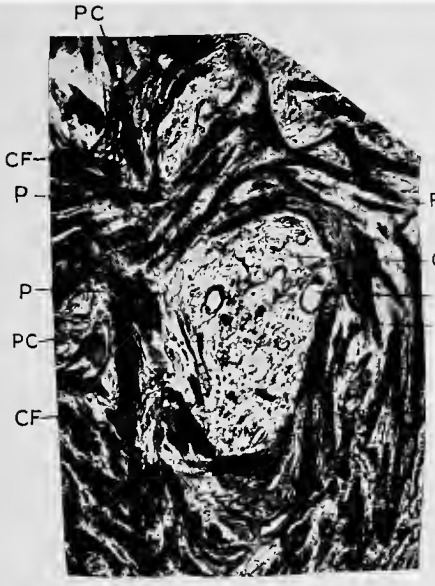
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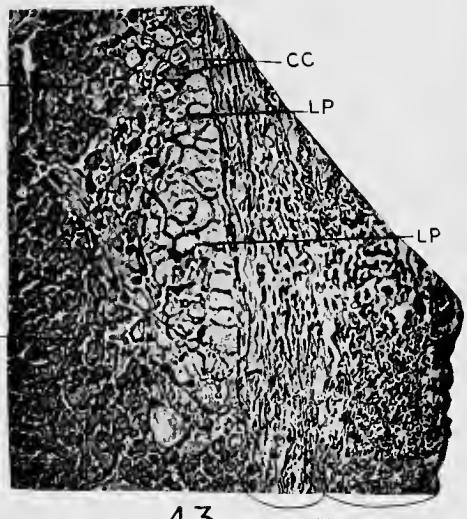
P
PC
CF
P
CTI
V
P

41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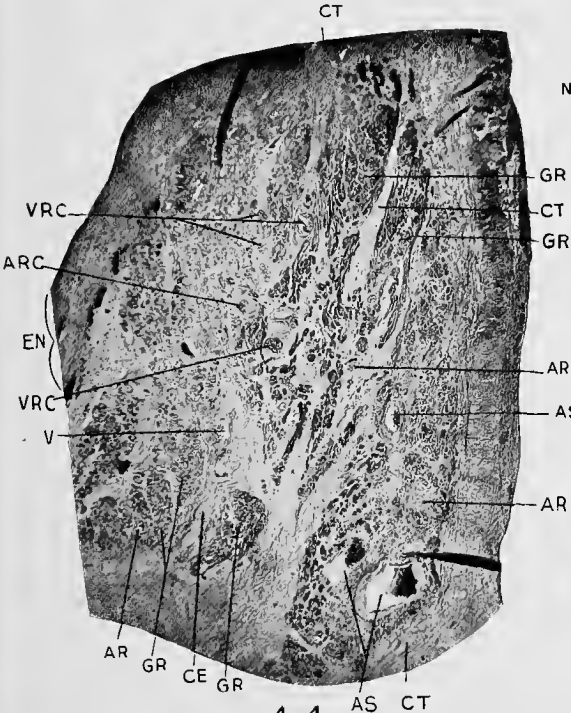
CC
LP
LP
LC
EN

43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VRC
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GR
ARC
EN
VRC
V
ARC
AS
AR
AR
GR
CE
GR
AS
CT

44


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NPC
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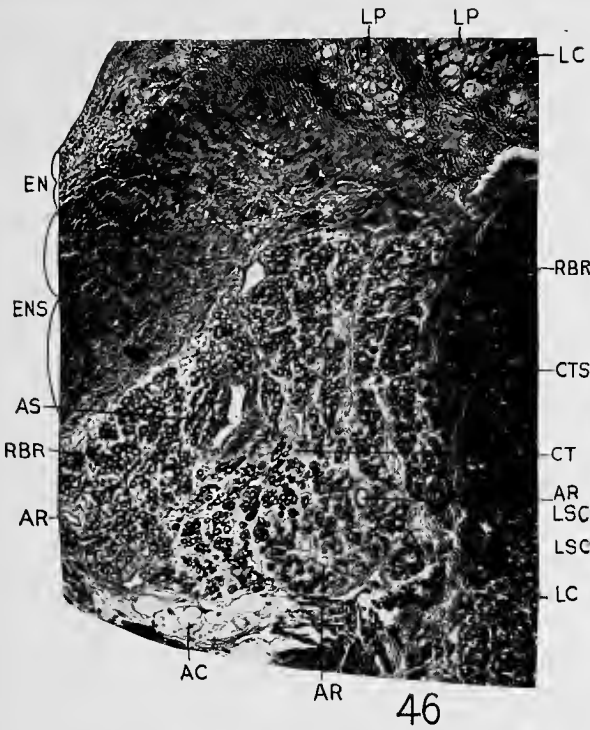
CPC
SA
PC
ID
SA
ID
NP II
PC
CT

42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AS
RBR
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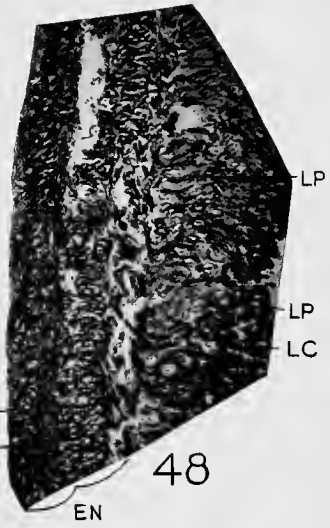
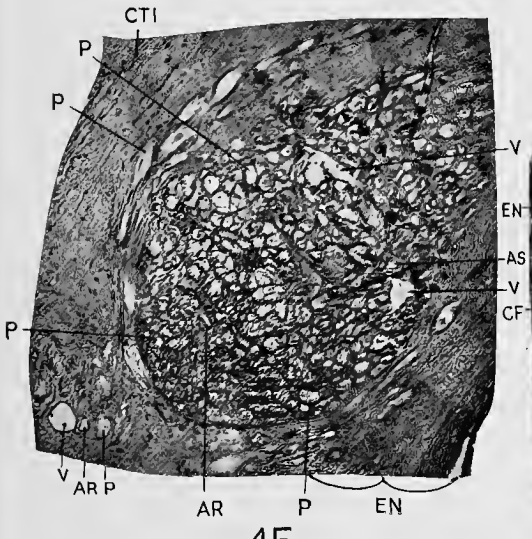
RBR
CTS
CT
AR
LSC
LSC
LC
AC
AR

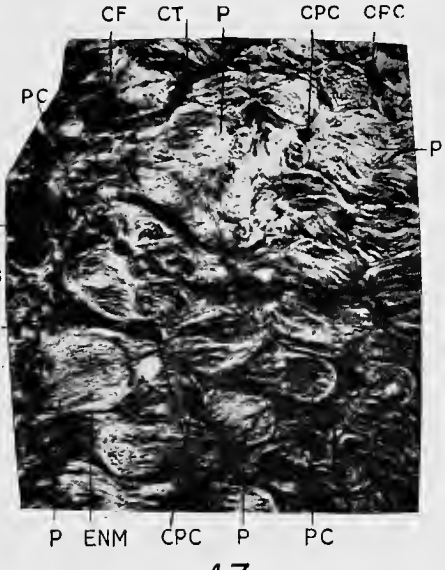
46


LP
LP
LC
EN

48


CTI
P
P
V
EN
AS
V
CF
P
V
AR
P
AR
P
EN

45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PC

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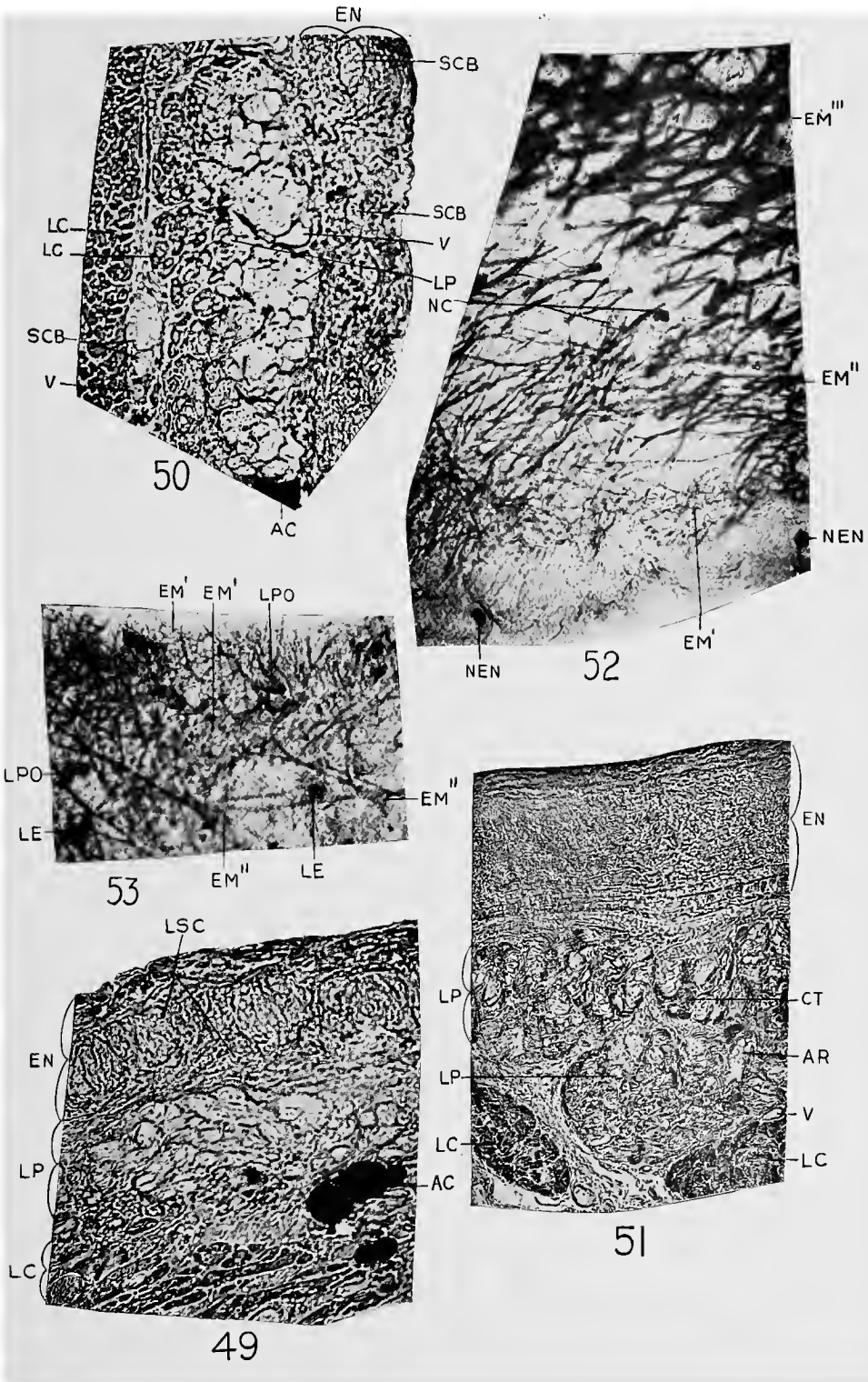
EN
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LC
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SCB
V
LP
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SCB
V
AC
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EM'''
EM''
NEN
EM'
NEN
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EM'
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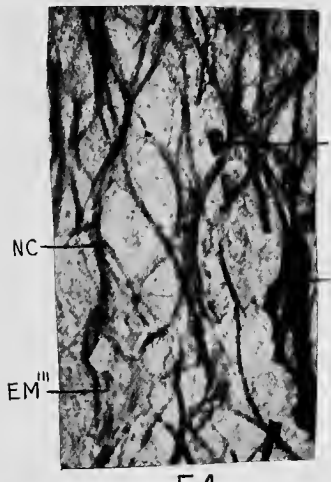

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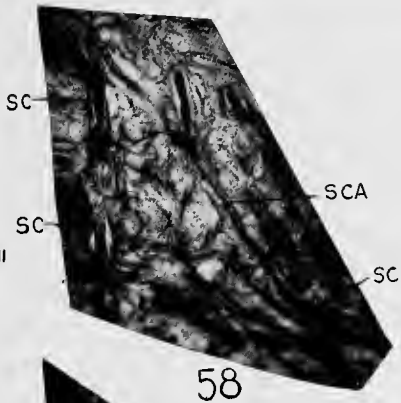

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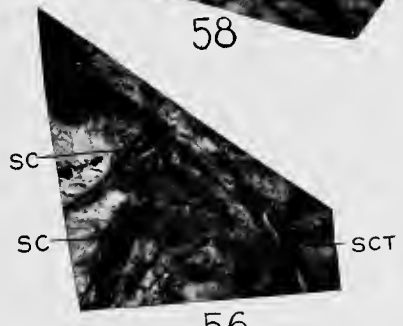

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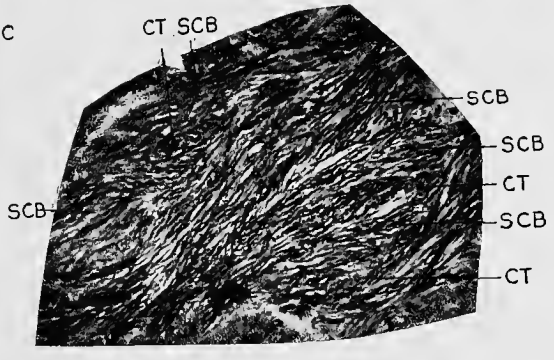

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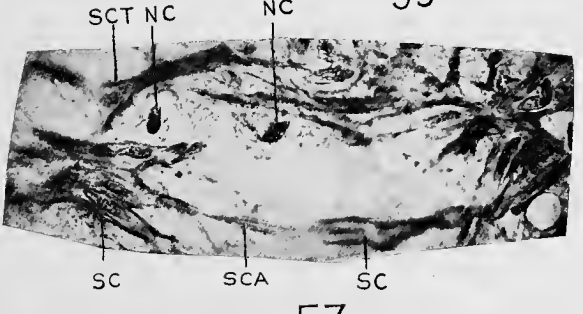

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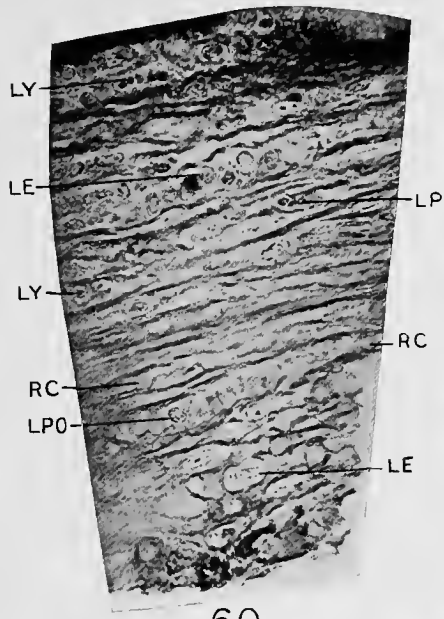

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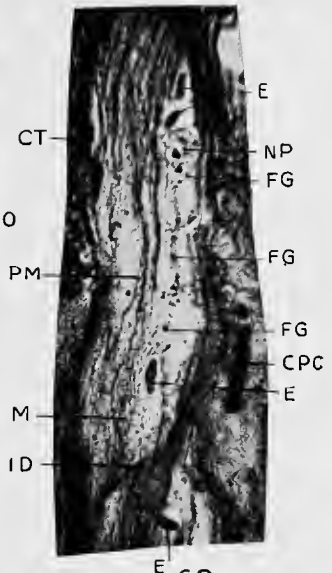

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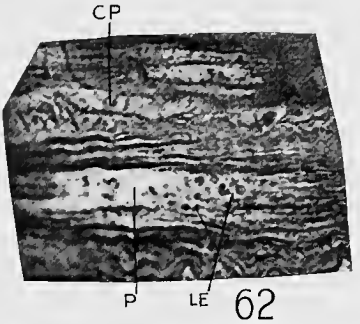

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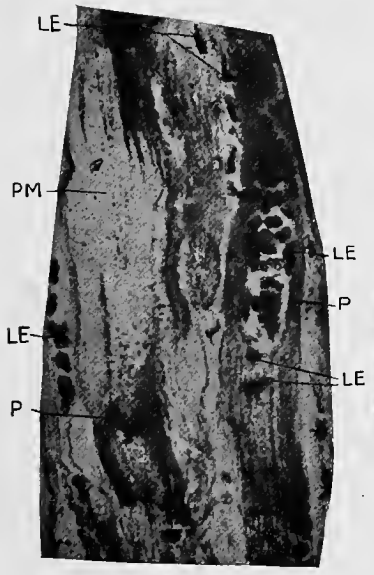

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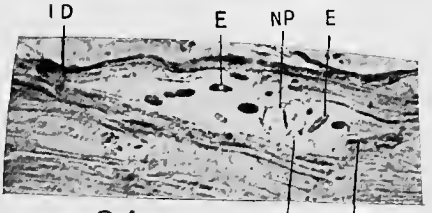

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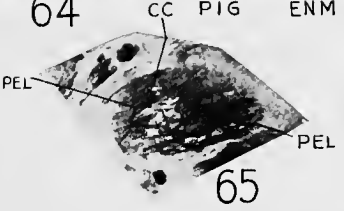

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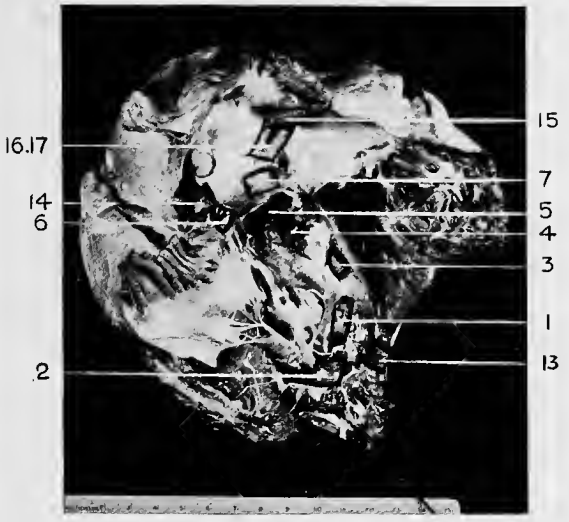

FIG-66.

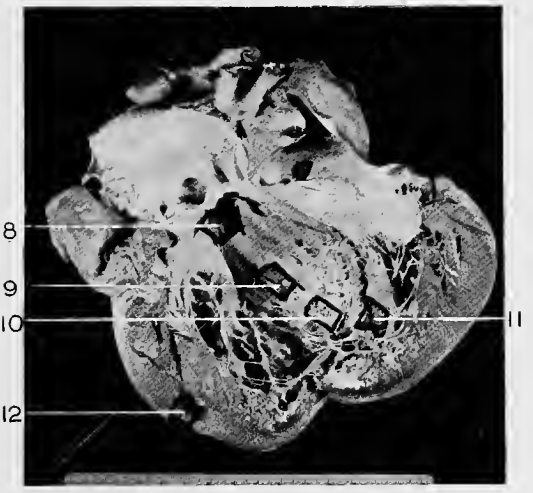

FIG-67.